EPA REGISTRATION NUMBER 2517-178

PROCESSING REQUEST

Reg # 2517 – RTF **Decision #**

Description:

Electronic Label & Letter (see PPLS):	OR	**Non Electronic Label & Letter** (Scanning required):
☐ Dated:		☐ Dated:

Only one label type should be selected

Other Materials Sent (see jacket):

☑ New CSF(s) Dated: all new

☐ Other:

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Autumn Metzger

Division: RD/IVB1

Phone: 305-5314 **Date:** 6/20/17

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration

(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
2517-178	6/15/17

Term of Issuance:
Conditional, Time-Limited
Expires: 06/15/2019

Name of Pesticide Product:
Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs

Name and Address of Registrant (include ZIP Code):
Sergeant's Pet Care Products, Inc.
10077 South 134th Street
Omaha, NE 68138

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A). You must comply with the following conditions:

1. Submit and/or cite all data required for registration/reregistration/registration review of your product under FIFRA when the Agency requires all registrants of similar products to submit such data.

Signature of Approving Official:
Sincerely,

Gene Benbow, Acting Product Manager 4
Invertebrate & Vertebrate Branch 1
Registration Division (7505P)
Office of Pesticide Programs

Date: 6/15/17

2. This registration is time-limited and expires 06/15/2019.

3. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product beginning within 3 months of the date the product is first released for shipment, on the first day of the quarter (i.e., January 1, April 1, July 1, or October 1). Please flag any Confidential Business Information as such. Submit enhanced incident reporting and quarterly sales information to the Product Manager's attention. The following is a list of information that must be included in the quarterly reports for each incident:

    - EPA Registration Number
    - Product name (brand name)
    - Lot #
    - Where purchased: internet, store, veterinarian
    - Active Ingredient(s)
    - Weight range for product
    - Date on which incident occurred (mm/dd/yyyy)
    - State in which the incident occurred (standard 2 letter abbreviation)
    - Registrant case #
    - Species: dog, cat, other (specify)
    - Breed: (as reported by pet owner)
    - Age: months or years
    - Sex: M, F, or neutered
    - Weight: pounds
    - Primary Route of Exposure: dermal, oral, other animal, inhalation, other
    - Body System: neurological, dermatological, GI, respiratory, ocular, other
    - Major signs noted with separate column for each sign, using standard terminology
    - Time to Onset: (hours, days)
    - Treated by veterinarian: yes or no
    - First time product used: yes or no
    - Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
    - Any known precondition
    - EPA Severity Code: death, major, moderate, minor
    - Outcome: died, recovered, still treated, unknown

4. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

    - All incidents should be reported including all minor dermal and ocular irritation reports.
    - Summary table for dogs showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.

- A similar summary table for cats (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for cats and table for dogs showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for dogs showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of dog incidents for each severity code for each pet weight range on the product label, as applicable.
- A summary table for dog weight showing number of incidents for each product weight range. This table should show number of incidents in dogs weighing less than that product weight range, number of incidents in dogs in lower half of weight range, number of incidents in dogs in upper half of weight range, and dogs weighing more than the product weight range, as applicable.
- Table showing number of incidents for each dog breed, where provided.
- Table showing number of incidents in dogs for each clinical sign.
- Table showing number of incidents in dogs for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If EPA determines that future mitigation measures are necessary for all pet spot-ons, the Agency will inform registrants. If mitigation measures are necessary, EPA may take regulatory action.

5. You are required to comply with the data requirements described in the DCIs identified below:

   a. Permethrin GDCI-109701-1252
   b. Imidacloprid GDCI-129099-951
   c. Pyriproxyfen GDCI-129032-1299

   You must comply with all of the data requirements within the established deadlines. If you have questions about the Generic DCIs listed above, you may contact the Chemical Review Manager in the Pesticide Reevaluation Division:
   http://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1

6. The data requirements for storage stability and corrosion characteristics (Guidelines 830.6317 and 830.6320) are not satisfied. A one year study is required to satisfy these data requirements. You have 18 months from the date of registration to provide these data.

7. Make the following label changes before you release the product for shipment:

   - Revise the EPA Registration Number to read, "EPA Reg. No. 2517-178."

8. Submit one copy of the final printed label for the record before you release the product for shipment.

Should you wish to add/retain a reference to the company's website on your label, then please be aware that the website becomes labeling under the Federal Insecticide Fungicide and Rodenticide Act and is subject to review by the Agency. If the website is false or misleading, the product would be misbranded and unlawful to sell or distribute under FIFRA section 12(a)(1)(E). 40 CFR 156.10(a)(5) list examples of statements EPA may consider false or misleading. In addition, regardless of whether a website is referenced on your product's label, claims made on the website may not substantially differ from those claims approved through the registration process. Therefore, should the Agency find or if it is brought to our attention that a website contains false or misleading statements or claims substantially differing from the EPA approved registration, the website will be referred to the EPA's Office of Enforcement and Compliance.

If you fail to satisfy these data requirements, EPA will consider appropriate regulatory action including, among other things, cancellation under FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Please note that the record for this product currently contains the following CSFs:

- Basic CSF dated 8/31/2016

If you have any questions, please contact Autumn Metzger at 703-919-7453, or Metzger.autumn@epa.gov.

Front panel **Dogs Squeeze On**

Permethrin + Imidacloprid + Pyriproxyfen

[Optional text appears in brackets/parenthesis – the final label may include some or all of the optional text on front, back or side label panels]

Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs

{Market Label-the word Dog will be at least 40-75% in height of the largest letter in the primary brand name.}
{Market Label-a large clear picture of a dog in the respective weight range will be on the front panel of the label for the product as packaged.}

{One of the following statements will appear on appropriate weight band market label on front panel as required per Agency's pet spot-on mitigation measures :}

For use ONLY on dogs [[&][and] puppies] [weighing] [4 [-][to] 10 lbs.][11 [-][to] 20 lbs.][21 [-][to] 55 lbs.][[more than][over][>] 55 lbs.] and over 7 weeks [old] [of age] {The appropriate weight class of dog will correspond to the appropriate pipette size}

For use ONLY on dogs [[&][and] puppies] [weighing] [4 [-][to] 10 lbs.] [11 [-][to] 20 lbs.][21 [-][to] 55 lbs.][[more than][over][>] 55 lbs.] and 7 weeks [of age] or older {The appropriate weight class of dog will correspond to the appropriate pipette size}

ONLY for dogs [[&][and] puppies]] over 7 weeks [old][of age]] and [weighing] [4 [-][to] 10 lbs.] [11 [-][to] 20 lbs.][21 [-][to] 55 lbs.][[more than][over][>] 55 lbs.] {The appropriate weight class of dog will correspond to the appropriate pipette size}

ONLY for dogs [[&][and] puppies]] 7 weeks [of age] or older and [weighing] [4 [-][to] 10 lbs.] [11 [-][to] 20 lbs.][21 [-][to] 55 lbs.][[more than][over][>] 55 lbs.] {The appropriate weight class of dog will correspond to the appropriate pipette size}

[1.5cm x 1.5cm on final as indicated][Lower right-hand corner front panel]{black cat/black text/red circle and line through cat/white background/ensure easy viewing on label}

{following text will be in addition to the above required language}

Small Dogs 4-10 lbs {only for use on label for 4-10 lbs and 7 weeks or older product}
Medium Dogs 11-20 lbs {only for use on label for 11-20 lbs and 7 weeks or older product}
Large Dogs 21-55 lbs {only for use on label for 21-55 lbs and 7 weeks or older product}
Extra Large Dogs >55 lbs {only for use on label for >55 lbs and 7 weeks or older product}
[Small][Medium][Large][Extra Large]

ACTIVE INGREDIENTS:

Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
OTHER INGREDIENTS:	46.76%
[TOTAL	100.00%]

*cis/trans ratio: Max 55% (±) cis and min 45% (±) trans

ACCEPTED
06/15/2017
Under the Federal Insecticide, Fungicide and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 2517-178

KEEP OUT OF REACH OF CHILDREN
WARNING

See [Back][or][Insert][Side][Label[s][Panel[s]] for Additional Precautionary Statements
[For Directions for Use, Storage and Disposal, and First Aid, see package insert inside.]

NET CONTENT: X fl oz [Y – X fl oz applicators]
[0.014 fl oz (0.4 mL) [tubes][vials][applicators][pipettes]]
[0.034 fl oz (1.0 mL) [tubes][vials][applicators][pipettes]]
[0.085 fl oz (2.5 mL) [tubes][vials][applicators][pipettes]]
[0.135 fl oz (4.0 mL) [tubes][vials][applicators][pipettes]]

{Begin Optional Active Ingredient Reference Statements}

[Compare to K9 Advantix® II active ingredients*]

[[Brand Name] [This product] contains [the] [same] [the] [active] ingredients [Imidacloprid, pyriproxyfen and permethrin,] used in
[K9 Advantix® II][K9 Advantix® II Small Dog] [K9 Advantix® II Medium Dog] [K9 Advantix® II Large Dog] [K9 Advantix® II Extra Large Dog]]*

[[Brand Name] [This product] contains Imidacloprid, pyriproxyfen and permethrin, the active ingredients used in
[K9 Advantix® II][K9 Advantix® II Small Dog] [K9 Advantix® II Medium Dog] [K9 Advantix® II Large Dog] [K9 Advantix® II Extra Large Dog]]*

{Note to reviewer: Text for footnote statement one}
[*[Brand Name] [This product] is not manufactured or distributed by Bayer Healthcare LLC, the makers of
[K9 Advantix® II][K9 Advantix® II Small Dog] [K9 Advantix® II Medium Dog] [K9 Advantix® II Large Dog] [K9 Advantix® II Extra Large Dog]]

{Note to reviewer: Text for footnote statement two}
**[K9 Advantix® II][K9 Advantix® II Small Dog] [K9 Advantix® II Medium Dog] [K9 Advantix® II Large Dog] [K9 Advantix® II Extra Large Dog]*
is a registered trademark of Bayer Healthcare LLC.]
{End Optional Active Ingredient Reference Statements}

[ABNs]
[AdvanceGuard Ticks2 for Dogs]
[SENTRY® AdvanceGuard Ticks2 for Dogs]
[Advanced Ticks 2 for Dogs]
[PetArmor® Advanced Ticks 2 for Dogs]
[DogMD Maximum Defense™ Advanced Ticks 2 for Dogs]
[DogMD Advanced Ticks 2 for Dogs]

{END - FRONT PANEL}

BACK PANEL/SIDE/INSERT PANEL **Dogs Squeeze On**
Imidacloprid + Permethrin + Pyriproxyfen

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES 7 WEEKS OF AGE OR OLDER.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS. WARNING. Causes substantial but temporary eye injury. Do not get in eyes or on skin or clothing. Harmful if swallowed. Harmful if absorbed through skin. Avoid contact with skin. Wash thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove and wash contaminated clothing before reuse.

HAZARDS TO DOMESTIC ANIMALS. For external use on dogs only. Do not use on animals other than dogs. Do not use on puppies under seven weeks of age or weighing less than [4] [11] [21] [55] lbs. Do not get this product in dogs' eyes or mouth. As with any product, consult your veterinarian before using this product on medicated, debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for dogs. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product.

{Side Effects box to be located on label above the cat prohibition icon/text all on the lower right hand side of the back panel}

Side Effects: Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or others side effects (such as lethargy or agitation) occur, consult your veterinarian or call 1-800-781-4738.

[1.5 cm x 1.5 cm on final or as indicated] [Lower right-hand corner back panel]

DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic organisms, including fish and invertebrates. Do not add directly to water. Do not contaminate water when disposing of product or packaging.

FIRST AID	
If In Eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If Swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on Skin or Clothing	• Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

HOT LINE NUMBER
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-781-4738 for emergency medical treatment information.
NOTE TO PHYSICIAN
Treat the patient symptomatically.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.
Do not contaminate feed or food.

How to Open:

1. Remove product tube[s] [vial[s]][applicator[s]][pipette[s]] from the package.
2. Separate one tube [vial][applicator][pipette] from the others. Hold the tube [vial][applicator][pipette] with notched end pointing up and away from the face and body. Use scissors to cut off the narrow end at the notches along the line.

How to Apply:

1. Invert tube [vial][applicator][pipette] over dog and use open end to part dog's hair.
2. Squeeze tube [vial][applicator][pipette] firmly to apply all of the solution to the dog's skin as a spot to the dog's back between the shoulder blades. [or] [from the back of the neck to a point midway between the neck and tail.]

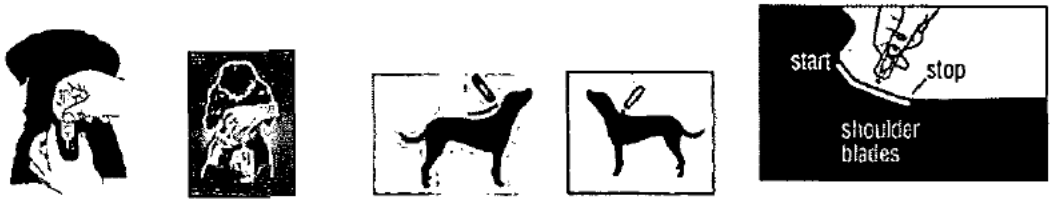
{For cartons containing 0.4 mL (0.014 fl oz) applicator tubes}
Only For Dogs Weighing 4 [-][to] 10 lbs. Do not apply to dogs weighing less than 4 lbs. [including small dogs and puppies, only 7 weeks or older] Apply one [tube][vial][applicator][pipette] 0.4 mL (0.014 fl oz) directly to skin [either] [as a spot [on] [to] the dog's back between the shoulder blades] [or] [as a [stripe] [line] starting from the back of the neck to a point midway between the neck and tail].

{For cartons containing 1.0 mL (0.034 fl oz) applicator tube}
Only For Dogs Weighing 11 [-][to] 20 lbs. Do not apply to dogs weighing less than 11 lbs.
Apply one tube[vial][applicator][pipette] 1.0 mL (0.034 fl oz) directly to skin [either] as a spot [on] [to] the dog's back between the shoulder blades [or] [as a [stripe] [line] starting from the back of the neck to a point midway between the neck and tail].

{For cartons containing 2.5 mL (0.085 fl oz) applicator tube}
Only For Dogs Weighing 21 [-][to] 55 lbs. Do not apply to dogs weighing less than 21 lbs.
Apply one tube[vial][applicator][pipette] 2.5 mL (0.085 fl oz) directly to skin [either] as a spot [on] [to] the dog's back between the shoulder blades [or] [as a [stripe] [line] starting from the back of the neck to a point midway between the neck and tail].

{For cartons containing 4.0 mL (0.135 fl oz) applicator tube}
Only For Dogs Weighing 55 lbs. or greater. Do not apply to dogs weighing less than 55 lbs. Do not use two [tube][vial][applicator][pipette]s on dogs greater than 55 lbs. Apply one tube[vial][applicator][pipette] 4.0 mL (0.135 fl oz) directly to skin [either] as a spot [on] [to] the dog's back between the shoulder blades [or] [as a [stripe][line] starting from the back of the neck to a point midway between the neck and tail].

[How to Apply - May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling. Refer to following optional graphics.]



FREQUENCY OF APPLICATION

[Use [Brand Name {or} this product] monthly for control of flea[s] [infestations].] [[Studies show that] [Brand Name {or} This product] kills fleas within 12 hours of application and [lasts {or} protects [for [up to] [[four][4] weeks][30 days][one month].]
[[Brand Name {or} This product] kills reinfesting fleas within [2][two] hours][two hours] and prevents further infestations of fleas [for [up to] [[four][4] weeks][30 days][one month]].]
[[Brand Name {or} This product] [targets multiple flea life stages] [and] [kills flea eggs and larvae before they develop into biting adults].]
[[Brand Name {or} This product] breaks the flea life cycle by killing flea eggs, flea larvae, and adult fleas.]
[If your dog is at high risk for flea reinfestation [, or in a highly infested environment], apply monthly.] [Apply monthly for flea control.]
[[Brand Name {or} This product] is waterproof and remains effective, even after bathing, swimming, or exposure to sunlight [and][or] [rain].] [Allow treated area to dry thoroughly.]

[PRODUCT INFORMATION]

[The successive feeding activity of fleas on dogs may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with this product [or ABN] rapidly kills fleas and may reduce the incidence of this condition.

This product [or ABN] kills existing fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting at least four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

This product [or ABN] is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.
Monthly treatments are required for optimal control and prevention of fleas and ticks.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: store in a cool, dry place. Protect from freezing.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Non-refillable container. **If empty:** Do not reuse or refill this container. Offer for recycling if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

[WARRANTY

Read the entire Directions for Use and Warranty before using this Product. By using this product, user or buyer accepts the following warranty. The directions for use of this product are believed to adequate and must be followed carefully. It is impossible to eliminate all risks associated with the use of this product. Unintended consequences may result because of unknown factors. All such risks shall be assumed by the user or buyer. Sergeant's is committed to providing high quality products. To the extent consistent with applicable law, Sergeant's makes no warranties, express or implied, of merchantability or of fitness for a particular purpose or otherwise, that extend beyond statements on this label. To the extent consistent with applicable law, Sergeant's, the manufacturer, or the Seller shall not be liable for indirect, special, incidental or consequential damages. To the extent consistent with applicable law, the exclusive remedy of the user or buyer shall not exceed the purchase price paid.]

[If you have questions or comments about this product, please write: [Sergeant's, Inc.] Consumer Response, P.O. Box 540399, Omaha, NE 68154-0399.]

[Satisfaction Guaranteed] [If you are not satisfied, we will make it right with a replacement or refund.]

In Case of Emergency, call: 1-800-781-4738
Non-Emergency, call: 1-800-224-PETS (7387)

[Coupon(s) inside or on outside of box]
[Made in USA With Global Materials]

[Distributed by:] [Manufactured by:]
Sergeant's Pet Care Products, Inc.
Omaha, NE 68138-3710

EPA Reg. No. 2517-RTI
EPA Est. No. XXXXX-XX-XX
[BAR CODE AREA]

{END - BACK/SIDE PANEL}

{START – ADDITIONAL OPTIONAL PACKAGE COPY OR FOLDED PANEL/FLAP OF FRONT OF PACKAGE OR INSERT}

[Clip. Part. Squeeze.]
[Easier-than-ever applicator lets you ***clip*** the tip, ***part*** the fur and ***apply*** directly to the skin – putting proven flea protection where it needs to be.]

[Application Instructions]
How to Open:

1. Remove product tube[s] [vial[s]][applicator[s]][pipette[s]] from the package.
2. Separate one tube [vial][applicator][pipette] from the others. Hold the tube [vial][applicator][pipette] with notched end pointing up and away from the face and body. Use scissors to cut off the narrow end at the notches along the line.

How to Apply:

1. Invert tube [vial][applicator][pipette] over dog and use open end to part dog's hair.
2. Squeeze tube [vial][applicator][pipette] firmly to apply all of the solution [on] [to] the dog's skin as a spot to the dog's back between the shoulder blades. [or] [from the back of the neck to a point midway between the neck and tail.]

Look at the Label [Easy] 6 Step [Easy] [Spot On] [Squeeze-On] [Topical] Checklist

- [1] Read the label completely and follow directions
- [2] Weigh your dog
- [3] Do NOT use dog products on cats
- [4] Do NOT treat with more than one pesticide product at a time
- [5] Separate animals after [treatment {or}application] to avoid chance of ingestion
- [6] Do NOT split [tube][vial][applicator][pipette] between dogs] [and use the ENTIRE [tube][vial][applicator][pipette] contents]

[Brand Name] [This product]
[Monthly reminder card]
[1][2][3][4][5][6] [12][24][Month [Treatment] [Application] Tracker][Carecard]
[For year-round protection, apply [Brand Name][this product] monthly.]
[Dog's Name (Empty blank for owner to fill in name)]
[Dog's Weight (Empty blank for owner to fill in name)]
[First][1st][Second][2nd][Third][3rd][Fourth][4th][Fifth][5th][Sixth][6th][Seventh][7th][Eighth][8th][Ninth][9th][Tenth][10th][Eleventh][11th][Twelfth][12th]
[Dose] [Treatment] [Application](Empty blank for owner to fill in date)(Date: MM/DD/YY)]
[Application Date][Date of Application]
[Calendar stickers with Brand Name]
[Place stickers on your calendar as a reminder to reapply [Brand Name][this product] [in 30 days.]
[Monthly Application Reminder Magnet (image of reminder magnet)]
[Place sticker on your calendar [or refrigerator] to remind yourself to apply [Brand Name][this product] to your dog]
[Enclosed for your convenience is an application reminder magnet. Push the (reset) button, and the reminder light will blink twice. The reminder tag is now set for 30 days. At the end of 30 days the reminder light will blink, reminding you to reapply [Brand Name][this product]. Press the button once and the blinking light will stop. Press the button again and this will reset the timer for another 30 days.]

[Each optional graphic below may or may not appear anywhere on the finished label]

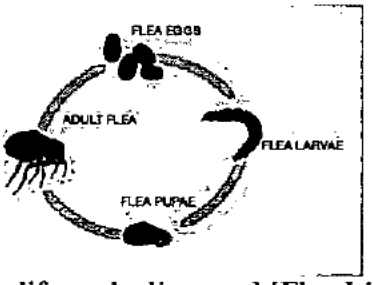
	Adult Flea	
	Fleas	
	Flea Eggs	
	Flea Larvae	
	Flea Pupae	
	Ticks	
	Deer Ticks	
	Brown Dog Ticks	
	Lone Star Ticks	
	American Dog Ticks	
	Lice	
	Biting Lice	
	Chewing Lice	
	Mosquitoes	
	Biting Flies	



[Waterproof]

MADE IN THE USA WITH GLOBAL MATERIALS

Good Housekeeping Promises



[Flea life cycle diagram] [Flea Life Cycle]

{non-mandatory optional graphics that may be used in addition to the EPA mandatory icon requirements that currently appear on the label.}

***Refund or replacement of product {text footnote to satisfaction guaranteed graphic}**

{END – ADDITIONAL OPTIONAL PACKAGE COPY OR FOLDED PANEL/FLAP OF FRONT OF PACKAGE OR INSERT}

TUBE/VIAL LABEL **Dogs Squeeze On**
Imidacloprid + Pyriproxyfen + Permethrin

{Front Label}	{Back Label}
Brand Name {for dogs} 4-10[11-20][21-55][>55] lbs. ≥7 wks Imidacloprid 8.8%, Permethrin 44%, Pyriproxyfen 0.44% 0.014 fl oz **(or)** 0.034 fl oz **(or)** 0.085 fl oz **(or)** 0.135 fl oz {label code}	KEEP OUT OF REACH OF CHILDREN WARNING Read directions and precautions on package. Use scissors to open. EPA REG. No. 2517-RTI {label code}

{EPA REG No may be on either the front or back label}
{Label code refers to Sergeant's product code number assignment to each product}

{END – TUBE/VIAL LABEL}

{Optional marketing statements below may or may not appear anywhere on the finished label]

[Flea/Flies Marketing Claims]
[Kills fleas]
[Repels and kills Fleas]
[Kills fleas on dogs]
[Active against fleas]
[Treats Fleas]

[Prevents Fleas]
[Repels biting flies]
[Controls against [irritating] flea bites]
[[Brand Name] Offers protection against fleas]
[Prevents and treats flea[s] [infestations]]
[Controls existing infestations by killing adult fleas]
[Controls existing flea infestation by killing adult fleas]
[Repels and kills fleas before they lay eggs]
[For the prevention and treatment of Flea Infestations]
[Prevents reinfestations by killing adult fleas before they lay eggs]
[Kills fleas even if your dog gets wet]
[May be used year-round for control of fleas]
[Controls fleas, which can serve as an intermediate tapeworm host]
[Repels, and inhibits blood-feeding by biting flies]
[Repels, and prevents blood-feeding by biting flies]
[[(prevents)(inhibits)] blood-feeding by biting flies]
[Repels [(annoying)(bothersome)(nuisance)] biting flies]
[Inhibits [(annoying)(bothersome)(nuisance)] biting flies]
[Kills reinfesting fleas within 2 hours [and protects against further infestation]]
[Kills fleas within 12 hours [of application][on dogs]]
[Kills fleas within 12 hours, continues to kill for 4 weeks]
[Kills fleas on dogs within 12 hours and continues to prevent infestations for [(a month) (four (4) weeks)]]
[Kills fleas within 12 hours on dogs [and prevents further infestations for [up to] [[4][four] weeks][[1][one][a] month]]
[One treatment prevents further flea infestations for [(a month) (four (4) weeks)]]
[Prevents further flea infestation for [[four][4] weeks][1 month] with one treatment]
[Prevents further flea infestation for [[four][4] weeks][1 month] with one application]
[[Brand Name] Prevents further flea infestation for [[four][4] weeks][1 month]]
[Once per month topical flea treatment for dogs]
[Once-a-month topical treatment for fleas on dogs]
[Prevents flea reinfestations for 30 days [1 month]]
[Prevents further flea infestations on dogs for 30 days [1 month]]
[Apply monthly [for effective flea control]]
[Apply monthly [to control and prevent fleas]]
[Monthly topical flea treatment for dogs]
[Monthly treatments are required for optimal control and prevention of fleas]
[The Only Flea Protection You Need For Your Dog[s] When Applied Monthly!]
[[Once per month][Monthly] topical flea treatment for dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Once per month][Monthly] topical flea treatment for dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Once-a-month topical treatment for fleas on dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Kills fleas on dogs and puppies 7 weeks or older and 4-10 or 11-20 or 21-55 or over 55 pounds [lbs]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs]
[Flea control for puppies and dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55

lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Flea control for puppies and dog 7 weeks [of age] or older] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Kills fleas, which may be a source of flea allergy dermatitis within 12 hours]
[Kills fleas that may cause flea allergy dermatitis, flea bite anemia, and tapeworm infestation]
[[Use of Brand Name][Use of this product] kills fleas and may reduce incidence of flea bite hypersensitivity] [and][or] [flea allergy dermatitis] [FAD]]
[[Use of Brand Name][Use of this product] kills fleas and may reduce incidence of [flea bite hypersensitivity] [and][or] flea allergy dermatitis [FAD]]
[Monthly treatment [with Brand Name][with this product] kills fleas and may reduce incidence of [flea bite hypersensitivity] [and][or] flea allergy dermatitis [FAD]]
[Monthly treatment [with Brand Name][with this product] kills fleas and may reduce incidence of flea bite hypersensitivity [and][or] [flea allergy dermatitis] [FAD]]
[Treatment with this product [or ABN] rapidly kills fleas and may reduce the incidence of Flea Allergic Dermatitis [FAD]]
[[Brand Name][This product] kills fleas and may reduce the incidence of a hypersensitivity skin disorder called flea allergy dermatitis (FAD), which may be caused by the feeding activity of fleas on dogs.]

[Ticks Marketing Claims]
[Kills Ticks]
[Treats Ticks]
[Prevents Ticks]
[Repels and kills Ticks]
[Repels and kills ticks including Deer ticks (vector of Lyme disease), American dog ticks (vector of Rocky Mountain spotted fever), Brown dog ticks (vector of Ehrlichiosis), and Lone Star ticks (vector of Ehrlichiosis), for up to four weeks]

[Mosquitoes Marketing Claims]
[Repels and kills Mosquitos]
[Repels and kills mosquitoes [for up to four weeks]
[Repels and kills mosquitoes often before they have a chance to take a blood meal]
[(Prevents blood-feeding by) (kills and repels)] mosquitoes]

[Lice Marketing Claims]
[Kills Lice]
[Kills [(biting)(chewing) lice]
[Controls existing [(biting)(chewing)] lice infestations]
[Kills [(biting)(chewing)] lice and prevents further infestations]
[Provides effective control of [(biting)(chewing) lice [infestations]]
[Treats, prevents and controls [(biting)(chewing) lice [infestations]]
[For treatment and prevention of [(biting)(chewing) lice [infestations]]
[For treatment and prevention of infestations with [(biting) (chewing)] lice]

[IGR Marketing Claims]
[Kills flea eggs]
[Controls existing flea eggs]
[Prevents flea eggs from hatching]
[Prevents flea eggs from developing into [biting] adult fleas]
[Prevents the development of flea eggs into [biting] adult fleas]
[[Brand Name][This product] contains Pyriproxyfen [PPF] [an insect growth regulator (IGR)] to kill flea eggs [and protect against reinfestation]]
[Prevents flea eggs [and flea larvae] from developing into [(biting)(adult)] fleas]
[Prevents development of fleas, flea eggs, pupae and larvae [for (a month)(four (4) weeks)]]
[Kills [flea eggs and] flea larvae]
[Kills flea eggs and flea larvae for up to four [4] weeks][1 month]]
[Controls existing flea eggs and fleas and prevents future infestations for 30 days [1 month]]
[Monthly treatment controls existing flea eggs and fleas and prevents future infestations]
[Kills multi-stages of fleas]
[Kills multiple flea life stages]
[Breaks the flea life cycle]
[Effectively breaks the flea life cycle]
[Targets multi-stages of flea lifecycle]
[Controls multi-stages of flea lifecycle]
[Repels and kills all [life] stages of fleas]
[Prevents development of all flea stages [for (a month)(four (4) weeks)]]
[Provides multi-stage flea control]
[Prevents multi-stages of the flea life cycle from developing]
[Effectively targets all [life] stages of [flea] and [ticks]]
[Brand Name] contains [an][the] [insect growth regulator] [IGR] [, Pyriproxyfen] [, in addition to Imidacloprid, and permethrin]
[This product [or ABN] contains [Imidacloprid], [permethrin] and [an/the] [insect growth regulator] [IGR] [Pyriproxyfen]

[COMBO Marketing Claims]
[Kills fleas before eggs can be laid]
[Treats ticks, fleas [and mosquitoes]]
[Prevents ticks, fleas [and mosquitoes]]
[Repels and kills ticks, fleas [and mosquitoes]]
[Flea Adulticide, larvicide and ovicide]
[[Brand Name][This product] is a flea ovicide, larvicide, and adulticide]
[Kills flea eggs, larvae, and [adult] fleas]
[Kills [adult] fleas, flea eggs, and flea larvae]
[Kills [adult] fleas, flea eggs and flea larvae for up to four [4] weeks][1 month]]
[Kills [adult] fleas, larvae, and eggs [, providing three-way protection]]
[3-way flea protection kills adults, larvae and eggs]
[3-way flea protection ([kills] [controls] adults, larvae, and eggs)]
[5-way protection (against fleas, ticks, biting flies, mosquitoes, and lice)]
[Topical prevention and treatment of ticks, fleas, mosquitoes, biting flies, and lice for monthly use.]
[This product [or ABN] is indicated for the prevention and treatment of fleas, ticks, biting flies, mosquitoes, and lice on dogs 7 weeks of age and older]

[All Other Marketing Claims]
[(Begins/Starts) working through contact]

[For use on dogs and puppies 7 weeks of age and older.]
[Apply to [dogs and] puppies over 7 weeks old and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Apply to [dogs and] puppies 7 weeks or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Formulated for Dogs and Puppies Over 7 Weeks [Old][of Age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Formulated for Dogs and Puppies 7 Weeks [of Age] or Older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Dogs and Puppies over 7 weeks [old][of age] [or] 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Can be used on puppies over 7 weeks [old][of age] [or] 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}

[Convenient]
[Easy application]
[Easy to apply product]
[Easy to Use [Application]]
[One Step Hassle Free Protection!]
[Convenient, easy to apply topical solution]
[Fragrance free]
[Waterproof]
[Remains effective even after the dog swims]
[Remains effective after bathing and/or swimming]
[Remains effective following swimming and/or shampooing]
[Remains effective after exposure to rain or sunlight]
[Remains effective, even after [bathing,][shampooing,] water immersion, or exposure to [sunlight] [and][or] rain]
[Once a month treatment]
[Apply once every [4 weeks] [month] [30 days]!]
[4 Week Dose!] [1 Month Dose!] [30 Day Dose!]
[Once a month topical flea treatment for dogs 7 weeks of age or older]
[A single topical application remains effective for [(a month) (four (4) weeks)]]

[One tube [vials][applicators][pipettes]]	[1 Month Supply]
[Two tube [vials][applicators][pipettes][pack]]	[2 Month Supply]
[Three tube [vials][applicators][pipettes][pack]]	[3 Month Supply]
[Four tube [vials][applicators][pipettes][pack]]	[4 Month Supply]
[Five tube [vials][applicators][pipettes][pack]]	[5 Month Supply]
[Six tube [vials][applicators][pipettes][pack]]	[6 Month Supply]
[9 tube [vials][applicators][pipettes][pack]]	[9 Month Supply]
[12 tube [vials][applicators][pipettes][pack]]	[12 Month Supply]
[24 tube [vials][applicators][pipettes][pack]]	[24 Month Supply]

[Direct to skin [tube][vial][applicator][pipette]]
[Easy to Use] [tube][vial][applicator][pipette]
[No-mess [open] [tube][vial][applicator][pipette]]
[Clip-tip design [tube][vial][applicator][pipette][!]]

[Consumer Value Marketing Claims]

[Coupon Inside]	[Sample size]
[Save Now!]	[Sample-Not for (re)sale]

[Value Size]	[Buy more and save!]
[Value pack]	[Buy X Get Y Free]
[Club Size]	[Buy 3[4] get 1 free]
[Bonus Size]	[(x)% (More) (Free)!]
[Club Pack]	[25 [33]% more free]
[Great Value]	[(x) Dose(s) Free!]
[Better Value]	[(x) Day(s) (Free)!]
[Bonus Pack]	[(x) Month(s) Free!]
[Bonus Buy]	[(x) Day(s) of treatment- Free!]
[[1][2][4][6][7][8][9][X] pack]	[(x) Tube(s) Free!]
[Twin Pack]	[(x) Applicator(s) Free!]
[Try Now, Save Later!]	[(x) Application(s) Free!]
[Z% Free]	[33% More Free]
[(x) + (x) bonus pack!]	[[New!] {only for use for 6 months from date of registration}]
[free sample]	

[Topical prevention and treatment of ticks, fleas, mosquitoes, biting flies, and lice for monthly use.]
[For the prevention and treatment of ticks, fleas, mosquitoes, biting flies, and lice on dogs.]
[The active ingredients in [Brand name][this product] are imidacloprid and pyriproxyfen. This product is formulated to control fleas [, flea eggs, and flea larvae] on dogs.] [[Brand Name][This product] kills fleas within 12 hours and prevents further flea infestations for [up to] [[4][four]weeks][[1][one] month][30 days].]

NOTE TO FILE

2517-RTI

6/20/2017

Even though the review states most of these MRIDs are unacceptable, all of the claims are considered acceptable since the product has cited identical efficacy studies as the parent and is "grand-fathered in"

This efficacy review was done in error (reviewer should not have beaned it since the data matrix was identical to the parent). It will be very useful for referring to data review for individual MRIDs listed on here and is still being filed in this jacket.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Autumn Metzger, MS

From: Tim Ciarlo, MS, Entomologist

Secondary Review: Jennifer Saunders, Ph.D., Senior Biologist

Date: May 4, 2017

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 436237
Decision no.: 521126
Submission no: 991754
Action code: R315
Product Name: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs
EPA File Symbol: 2517-RTI
Formulation Type: Spot-On
Ingredients statement from the label with PC codes included:

Imidacloprid	8.8%	PC: 129099
Permethrin	44.0%	PC: 109701
Pyriproxyfen	0.44%	PC: 129032

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate):

For dogs weighing 1.81-4.54 kg (4-10 lbs):	0.4 ml product (99.3-248.3 mg product/kg body weight)
	8.8-21.8 (avg. 15.3) mg imidacloprid/kg body weight
	43.7-109.3 (avg. 76.5) mg permethrin/kg body weight
	0.44-1.09 (avg. 0.77) mg pyriproxyfen/kg body weight
For dogs weighing 4.99-9.07 kg (11-20 lbs):	1.0 ml product (124.1-225.7 mg product/kg body weight)
	10.9-19.8 (avg. 15.35) mg imidacloprid/kg body weight
	54.6-99.2 (avg. 76.9) mg permethrin/kg body weight
	0.55-0.99 (avg. 0.77) mg pyriproxyfen/kg body weight
For dogs weighing 9.53-24.95 kg (21-55 lbs):	2.5 ml product (112.8-295.5 mg product/kg body weight)
	9.9-26.0 (avg. 17.95) mg imidacloprid/kg body weight
	49.6-130.0 (avg. 89.8) mg permethrin/kg body weight
	0.50-1.30 (avg. 0.9) mg pyriproxyfen/kg body weight
For dogs weighing >24.95 kg (>55 lbs):	4.0 ml product (82.6*-180.5 mg product/kg body weight)
	7.3*-9.9 (avg. 8.6) mg imidacloprid/kg body weight
	36.3*-49.6 (avg. 42.95) mg permethrin/kg body weight
	0.36*-0.50 (avg. 0.43) mg pyriproxyfen/kg body weight

*The lower end of the dose range for this weight class is based on a 54.54 kg dog which is not reflected on the label. A large dog of 54.54 kg is needed to calculate a conservative dose from an efficacy perspective.

Use Patterns: Monthly topical treatment for dogs to kill fleas, ticks, mosquitoes, lice, and prevent fleas from developing into adults.

I. Action Requested: The Risk Manager requests review of 15 cited MRIDs to determine if efficacy against fleas, ticks, mosquitoes, and lice is supported for 2517-RTI.

II. Background: The Agency previously reviewed several of the MRIDs being cited with this action in the context of other products (DPs 428232, 428138,425605, 430187). Several of the reviews below are taken from previous reviews and tailored to 2517-RTI accordingly.

III. MRID Summary:

44256901. Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs.

(1) GLP

(2) **Methods:** Thirty dogs were divided into three groups of ten, and dogs in each group received one of the following treatments: 9.1% imidacloprid per label instructions (see table 1 below), 9.7% fipronil per label instructions (see table 2 below), or a placebo control. Dogs were subsequently split into 5 subgroups of two within each treatment. Assuming the formulation density of the proposed product is similar to that of the tested product, the rate of imidacloprid tested in the study is the same as the rate on the proposed product. Note the mean dose tested is 16.75 mg imidacloprid/kg body weight (range of doses tested is approximately 10.9 - 24 mg imidacloprid/kg body weight) if the density assumption is correct. Dogs were infested with 100 adult cat fleas on days -1, 6, 13, 20, and 27. On day 0, fleas were evaluated as live, moribund, or dead on different subgroups of two dogs from each treatment at each of 2, 4, 8, 12, and 24 h post treatment, and on days 6, 13, 20, and 27 flea evaluations were performed in the same way at the same time intervals post infestation. Live and moribund fleas were collected and held in a separate container for 24 hours to assess mortality.

Table 1. Imidacloprid dosing instructions.

Dog Size	Dose
10 lb and under	0.4 mL
11 - 20 lbs	1.0 mL
21 - 55 lbs.	2.5 mL
Over 55 lbs.	4.0 mL

Table 2. Fipronil dosing instructions.

Dog Size	Dose
up to 22 lbs.	0.67 mL
23 - 44 lbs.	1.34 mL
45 - 88 lbs.	2.68 mL

(3) **Results:** Mortality of fleas exposed to the imidacloprid treatment on dogs for 8 hours or more was over 90% on all evaluation dates except on day 0 and 27. On day 0, mortality of fleas exposed to imidacloprid for 8 hours was 89%, and on day 27 mortality of fleas exposed for 12 hours was 81.5%. However on day 27, mortality of fleas

exposed to imidacloprid for 4 hours was 98% and the lower control at 12 hours was the result of increased survival on 1 of the 2 dogs evaluated at 12 hours post infestation. Mortality of fleas exposed to imidacloprid on treated dogs for less than 4 hours did not consistently reach 90% across evaluation dates and replication at each evaluation time point is not adequate for statistical significance. Mortality of fleas exposed to fipronil treated dogs for 8 hours or more was over 90% on all evaluation dates; however, flea mortality when exposed for 2 or 4 hours did not consistently reach 90% across evaluation dates.

(4) **Conclusion: Partially Acceptable.** This study supports claims of kills fleas at the label rate of 16.75 mg imidacloprid/kg body weight for the proposed imidacloprid product because acceptable efficacy was consistently found on at least 6 dogs (the combined sample size of groups with fleas exposed for over 8 hours). However, this study does not support "speed of kill" claims because the sample size of dogs evaluated at each time point (2) was not adequate to show statistical significance of the treatment at any time point. In addition, statistical analyses were not performed. To support "speed of kill" claims, mortality in the treated group should be significantly different from mortality in the control group at the desired time point after statistical analysis.

44256902. Imidacloprid Topical Formulation Larvacidal Effect Against *Ctenocephalides felis* in the Surroundings of Treated Dogs.

(1) non-GLP

(2) **Methods:** This MRID includes two studies which are intended to assess flea larvicidal efficacy of an imidacloprid dog spot-on product. In the first study, two dogs were treated with an imidacloprid spot-on formulation on day 0 at an application rate of 10 mg imidacloprid/kg. Two other dogs were included as the untreated control group. On days 1 and 7, one dog from each of the two groups were confined to a cage for 1 hour. After this 1-hour period, debris which had fallen from each dog was collected from a tray below each cage. This procedure was repeated with the other two dogs on days 2, 14, 21, and 28. After all hair was removed from each debris sample, 5-10 mg of debris was added to a petri dish along with 10 mg of dried bovine blood and 22 unhatched flea eggs. Petri dishes were placed in an incubator (23.5-26.5°C) in the dark at 75-92% relative humidity. The number of live fleas in each petri dish was recorded at 4 hours and then daily for 9 days post-inoculation. Debris collected on days 2 and 7 was re-tested on days 61 and 51, respectively, although it is not clear how long flea eggs/larvae were exposed to debris on these later days and when live flea counts were recorded. Percent mortality was corrected for mortality in the untreated control group using Abbott's formula:

Corrected larval mortality = (observed mortality – control mortality) / (100 – control mortality)

In the second study, four dogs were infested with 100 adult fleas twice weekly for 4 weeks. After the second and each subsequent infestation, two of the dogs were placed in a 1.6 x 2.5 m room (Room A) for 2 hours, and two were placed in an identical adjacent room (Room B) with the intention of seeding both rooms with flea eggs. The floor of both rooms was covered with sawdust to create a favorable larval environment. Three other dogs were treated with an imidacloprid spot-on formulation on day 0 at an application rate of 10 mg/kg. These dogs were placed into Room B for one hour each 5 days a week, starting 1 day after the untreated "seed" dogs had been introduced for the first time. After 18 days from the first "seeding" event, 5 samples of sawdust (total weight: 88.56 g) were collected from the floor of Room A, and 5 were collected from Room B (total weight: 95.82 g). Of the 5 samples, 4 were taken from the corners of each room, and 1 was taken from the center. Each sample was placed in a petri dish with 500 mg of bovine blood and 100 flea eggs.

Seven and 11 days after these samples were collected and seeded with flea eggs, 2 of the 5 samples from each room were counted for live flea larvae. The remaining petri dish samples from each room were then aggregated into larger treated and control samples and counted for pupae 23 days after sample collection. On day 29, 193 g samples were taken from the floor of each room and counted for live immature fleas. On day 42, a technician wearing white coveralls moved around each room and counted the number of adult fleas jumping onto his/her legs. The number of larvae and pupae were compared at the above time points, as well as the number of adult fleas counted during the whitewalker trial.

This MRID contains two studies, one which used only four dogs for testing, and a second study which used seven dogs split into two groups. Because neither study was adequately replicated, this study was not evaluated further.

(3) Results: Percent larval mortality from flea egg/larvae exposure to treated dog debris is summarized in Table 1 below:

TABLE 1. Mortality of *Ctenocephalides felis* larvae in contact with 5 to 10mg of debris falling in 1 hour from dogs at various times after treatment with imidacloprid 10% w/v topical formulation at 10mg/kg.

	DAYS AFTER TREATMENT						RETESTED SAMPLES	
							Day 7 samples	Day 2 samples
	1	2	7	14	21	28	51 days later	61 days later
PERCENT MORTALITY	100	98.8 no pupae*	100	100	95.3** no pupae	100	100	97.4*** no pupae

Percent larval mortality was reported as 100%, 98.8%, 100%, 100%, 95.3%, 100%, 100%, and 97.4% at 1, 2, 7, 14, 21, 28, 51, and 61 days post treatment. However, raw data were not provided, and mortality in the control group could not be determined.

The number of flea larvae/pupae/adults at various time points in the second study are summarized in Table 2 below:

TABLE 2. Number * of larvae, pupae and adult, *Ctenocephalides felis* 741

In two identical rooms naturally contaminated with flea eggs from infested dogs.

Dogs treated with imidacloprid topical at 10mg/kg had access to Room B

for 3 hours per day over 15 days.

Sample	Time of sampling	Origin of sample		Difference
		Room A without access by imidacloprid treated dogs *	Room B exposed to imidacloprid treated dogs *	Percent efficiency
Floor sawdust from the rooms. Artificially seeded with flea eggs. In dishes	7 days after eggs added	58 early stage larvae in 96g	5 larvae in 96g	91%
	11 days	1972 larvae in 99g	84 larvae in 99g	96%
	23 days	711 pupae in 51g	7 pupae in 51g	99%
Floor sawdust in the rooms (Infested dogs entered first on day 1)	Day 29	47 larvae 83 pupae in 193g	8 larvae in 193g	87% 100%
	Day 42	94 fleas in 14 seconds on a person moving around the room.	3 fleas in 12 minutes	97%

* Numbers corrected to same sample size.

(4) **Conclusion: Unacceptable.** Neither study in this MRID was replicated adequately. The Agency recommends a minimum of six animals per treatment group for sufficient replication and statistical power. Raw data should be provided. Control mortality should not exceed 10%.

44256903. Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs.

(1) GLP

(2) **Methods:** Twenty-four dogs were divided into three groups. Two groups (1, 2) were treated with a 9.1% imidacloprid spot-on product (**Group 1**: dose range: 11.0-25.5 mg imidacloprid/kg body weight, Average dose: 16.1 mg imidacloprid/kg body weight; **Group 2**: Dose range: 11.4-17.8 mg imidacloprid/kg body weight, Average dose: 14.5 mg imidacloprid/kg body weight) and group 3 served as the untreated control group. Dogs were infested with

100 adult fleas on days -1, 6, 13, 20, 27, and 34. Live fleas were counted and removed from the dog on days 1, 7, 14, 21, 28, and 35. On day 4, all dogs in group 1 and 4 dogs from group 3 were shampooed and rinsed, and all dogs in group 2 and 4 dogs from group 3 were immersed in a tank of water for one minute. During the one minute immersion period, the study staff dunked the dogs heads under water three times. All dogs immersed in water on day 4 were also immersed in the same manner on days 11, 18, 25 and 32.

(3) **Results:** Over 90% mortality of fleas on dogs in group 1 was observed through day 28. On day 35, flea mortality only reached 65.5% on dogs in group 1. Mortality of fleas on dogs in group 2 was over 90% through 14 days post treatment, 89.7% on day 21, 88.8% on day 28, and 78.7% on day 35.

(4) **Conclusion: Partially Acceptable**. This study supports claims of kills fleas at the dose rate of 16.1 mg imidacloprid/kg body weight because efficacy in group 1 was over 90% through 28 days post application. Furthermore, this study supports that the subject product maintains efficacy against fleas after swimming/exposure to rain/water immersion for 3 weeks at the aforementioned dose rate. Claims that 2517-RTI withstands shampooing/bathing and maintains efficacy against fleas are not supported at the aforementioned dose rate. Animals undergoing shampoo/bathing resistant tests should be shampooed with a non-medicated shampoo and then rinsed for at least 5 minutes using a minimum of a 3.0 gallon per minute showerhead. The shampoo/rinsing procedures in MRID 44256903 were inadequately detailed for these parameters to be determined. Moreover, although the test substance contains nearly the same amount of imidacloprid as the subject product, the inert/other ingredients differ; the extent of these formulation differences is not known. Because inert/other ingredients may play such a large role in spot-on product characteristics like shampoo resistance, efficacy testing to support these type of claims should be conducted with the formulated product itself.

45563011. Efficacy of Topically Applied Imidacloprid + Permethrin against Flea (*Ctenocephalides felis*) and Tick (*Rhipicephalus sanguineus*) Infestations on Dogs.

(1) GLP

(2) **Methods:** Forty dogs were divided into 4 groups of 10 in a randomized block design, and dogs in each group received one of the following topical treatments:

1. G804S19 – 7.12% imidacloprid + 35.66% permethrin (see Table 1 below)
2. G804S16 – 8.80% imidacloprid + 44.00% permethrin (see Table 2 below)
3. Advantage® - 9.1% imidacloprid (see Table 2 below)
4. G804S40 – Placebo control – G804S16 minus active ingredients (see Table 2 below)

Table 1: Dosing instructions for G804S19

Dosages for G804S19	
For Dogs ≤ 10 lbs.	0.5 mL
For Dogs 10.1 - 20 lbs.	1.25 mL
For Dogs 20.1 - 55 lbs.	3.125 mL
For Dogs > 55 lbs	5.0 mL

Table 2: Dosing instructions for G804S16, Advantage®, and G804S40

Dosages for G804S16, Advantage and G804S40	
For Dogs ≤ 10 lbs.	0.4 mL
For Dogs 10.1 - 20 lbs.	1.0 mL
For Dogs 20.1 - 55 lbs.	2.5 mL
For Dogs > 55 lbs	4.0 mL

Dogs were ranked after a pre-study flea count. The 4 dogs with the highest flea counts were assigned to Block 1, the next 4 dogs were assigned to Block 2, and so on such that the 4 dogs with the lowest flea counts were assigned to the

final Block. Dogs from each Block were then assigned 1 of the 4 treatments described above. This randomization procedure was repeated for each sex so that each of the 4 treatment groups had 5 males and 5 females.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation G804S19, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **18.67 mg imidacloprid/kg body weight** (range of doses tested is 13.72-27.21 mg imidacloprid/kg body weight) and **93.49 mg permethrin/kg body weight** (range of doses tested is 68.73-136.27 mg permethrin/kg body weight) if the density assumption is correct.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation G804S16, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **16.01 mg imidacloprid/kg body weight** (range of doses tested is 11.15-24.27 mg imidacloprid/kg body weight) and **80.05 mg permethrin/kg body weight** (range of doses tested is 55.73-121.36 mg permethrin/kg body weight) if the density assumption is correct.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of Advantage®, the rate of imidacloprid tested with this formulation is within the rate on the proposed product label. Note the mean dose tested is **19.42 mg imidacloprid/kg body weight** (range of doses tested is 12.34-26.64 mg imidacloprid/kg body weight) if the density assumption is correct. Imidacloprid is the only active ingredient in Advantage®.

A single application of 1 of the 4 treatments described above was made to each dog on day 0. Dogs were infested with 100 adult cat fleas on days -5, -1, 6, 13, 20, 27, 34, and 41. Dogs were infested with 50 adult Brown Dog ticks on days -6, -2, 5, 12, 19, 26, 33, and 40. On days -5, 2, 7, 14, 21, 28, 35, and 42, live fleas and attached, live ticks were counted and removed from each dog using combs and forceps. Abbott's formula was used to calculate percent control for each treatment group:

$$\% \text{ Control} = [(X - Y) / X] (100)$$

Where: X = Geometric mean of fleas or ticks from control animals
Y = Geometric mean of fleas or ticks from treated animals

(3) **Results:**

Placebo Control: Mean flea counts in the placebo control group were reported as 75.7, 73.5, 82.0, 82.9, 73.9, 73.7, 84.8, and 78.2 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively, indicating an adequate level of flea infestation in the control group. Mean attached tick counts in the placebo control group were reported as 24.3, 29.6, 32.8, 31.2, 20.6, 19.9, 22.6, and 22.5 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively, indicating an adequate level of tick infestation in the control group.

G804S19: Mean flea counts were reported as 78.8, 0.0, 0.0, 0.0, 0.2, 0.7, 9.5, and 8.1 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 20.6, 1.8, 0.0, 0.2, 0.5, 1.4, 3.2, and 3.1 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100%, 100%, 100%, 99.8%, 99.5%, 96.0%, and 95.7% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 95.9%, 100.0%, 99.5%, 98.2%, 95.0%, 88.6%, and 89.3% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

G804S16: Mean flea counts were reported as 78.4, 0.0, 0.0, 0.0, 3.5, 3.0, 7.9, and 5.3 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 26.3, 3.8, 0.0, 0.4, 0.5, 1.7, 3.2, and 3.7 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100.0%, 100.0%, 100.0%, 99.3%, 99.3%, 97.0%, and 97.6% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 90.8%, 100.0%, 99.0%, 97.9%, 94.6%, 89.1%, and 87.8% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

Advantage®: Mean flea counts were reported as 77.6, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, and 0.2 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 24.3, 7.0, 3.3, 10.3, 8.3, 18.4, 23.2, and 18.1 on days -5, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100%, 100%, 100%, 100.0%, 100.0%, 100.0%, and 99.8% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 80.7%, 95.7%, 77.7%, 69.9%, 28.9%, 3.8%, and 46.2% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

(4) **Conclusion: Acceptable.** This study supports that 2517-RTI kills fleas on dogs for up to 42 days/6 weeks at the dose rate of 16.01 mg imidacloprid/kg body weight and 80.05 mg permethrin/kg body weight because efficacy in both G804S19- and G804S16-treated groups was over 90% through 42 days post application.

This study supports that 2517-RTI kills Brown Dog ticks on dogs for up to 28 days/4 weeks/1 month at the dose rate of 16.01 mg imidacloprid/kg body weight and 80.05 mg permethrin/kg body weight because efficacy in the G804S16-treated group was over 90% through 28 days post application.

This study supports that 2517-RTI kills Brown Dog ticks on dogs for up to 35 days/5 weeks at the slightly higher dose rate of 18.67 mg imidacloprid/kg body weight and 93.49 mg permethrin/kg body weight because efficacy in the G804S19-treated group was over 90% through 35 days post application.

Tick claims cannot be supported by this study alone, as efficacy should be demonstrated against Brown Dog ticks (*R. sanguineus*), American Dog ticks (*Dermacentor variabilis*), and Blacklegged ticks (*Ixodes scapularis*). This study may be combined with other studies to support a tick claim, however.

45573501. Efficacy of Topically Applied Imidacloprid + Permethrin against Flea (*Ctenocephalides felis*) and Tick (*Amblyomma americanum*) Infestations on Dogs.

(1) GLP

(2) **Methods:** Forty dogs were divided into 4 groups of 10 in a randomized block design, and dogs in each group received one of the following topical treatments:

1. G804S19 – 7.12% imidacloprid + 35.66% permethrin (see Table 1 below)
2. G804S16 – 8.80% imidacloprid + 44.00% permethrin (see Table 2 below)
3. Advantage® - 9.1% imidacloprid (see Table 2 below)
4. G804S40 – Placebo control – G804S16 minus active ingredients (see Table 2 below)

Table 1: Dosing instructions for G804S19

Dosages for G804S19	
For Dogs ≤ 10 lbs.	0.5 mL
For Dogs 10.1 - 20 lbs.	1.25 mL
For Dogs 20.1 - 55 lbs.	3.125 mL
For Dogs > 55 lbs	5.0 mL

Table 2: Dosing instructions for G804S16, Advantage®, and G804S40

Dosages for G804S16, Advantage and G804S40	
For Dogs ≤ 10 lbs.	0.4 mL
For Dogs 10.1 - 20 lbs.	1.0 mL
For Dogs 20.1 - 55 lbs.	2.5 mL
For Dogs > 55 lbs	4.0 mL

Dogs were ranked after a pre-study flea count. The 4 dogs with the highest flea counts were assigned to Block 1, the next 4 dogs were assigned to Block 2, and so on such that the 4 dogs with the lowest flea counts were assigned to the final Block. Dogs from each Block were then assigned 1 of the 4 treatments described above. This randomization procedure was repeated for each sex so that each of the 4 treatment groups had 5 males and 5 females.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation G804S19, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **17.65 mg imidacloprid/kg body weight** (range of doses tested is 13.60-24.88 mg imidacloprid/kg body weight) and **88.41 mg permethrin/kg body weight** (range of doses tested is 68.14-124.61 mg permethrin/kg body weight) if the density assumption is correct.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation G804S16, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **15.19 mg imidacloprid/kg body weight** (range of doses tested is 11.15-20.38 mg imidacloprid/kg body weight) and **75.95 mg permethrin/kg body weight** (range of doses tested is 55.73-101.89 mg permethrin/kg body weight) if the density assumption is correct.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of Advantage®, the rate of imidacloprid tested with this formulation is within the rate on the proposed product label. Note the mean dose tested is **16.10 mg imidacloprid/kg body weight** (range of doses tested is 11.01-21.31 mg imidacloprid/kg body weight) if the density assumption is correct. Imidacloprid is the only active ingredient in Advantage®.

A single application of 1 of the 4 treatments described above was made to each dog on day 0. Dogs were infested with 100 adult cat fleas on days -8, -1, 6, 13, 20, 27, 34, and 41. Dogs were infested with 50 adult lone star ticks on days -9, -2, 5, 12, 19, 26, 33, and 40. On days -7, 2, 7, 14, 21, 28, 35, and 42, live fleas and attached, live ticks were counted and removed from each dog using combs and forceps. Abbott's formula was used to calculate percent control for each treatment group:

$$\% \text{ Control} = [(X - Y) / X] (100)$$

Where: X = Geometric mean of fleas or ticks from control animals
Y = Geometric mean of fleas or ticks from treated animals

(3) **Results:**
Placebo Control: Mean flea counts in the placebo control group were reported as 60.3, 35.9, 78.4, 73.9, 77.7, 84.8, 78.5, and 68.4 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively, indicating an adequate level of flea infestation in the control group. Mean attached tick counts in the placebo control group were reported as 16.7, 3.6, 4.8, 2.1, 1.3, 5.6, 4.2, and 3.6 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Of the 50 ticks placed on each dog at each infestation point, only 33% were attached on day -7, and only 4-11% were attached on the remaining count days.

G804S19: Mean flea counts were reported as 60.9, 0.0, 0.1, 0.0, 0.1, 0.4, 1.9, and 2.6 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 14.0, 1.2, 0.0, 0.0, 0.0, 0.5, 0.2, and 0.4 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100.0%, 99.9%, 100.0%, 99.9%, 99.6%, 99.2%, and 98.0% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 77.6%, 100.0%, 100.0%, 100.0%, 92.0%, 96.9%, and 89.7% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

G804S16: Mean flea counts were reported as 62.1, 0.0, 0.0, 0.0, 0.2, 0.8, 2.9, and 2.3 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 15.1, 3.3, 3.2, 2.7, 0.7, 4.4, 5.9, and 3.2 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100.0%, 100.0%, 100.0%, 99.8%, 99.5%, 98.5%, and 98.5% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 48.6%, 100.0%, 100.0%, 100.0%, 79.5%, 93.9%, and 44.0% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

Advantage®: Mean flea counts were reported as 61.8, 0.0, 0.1, 0.0, 0.4, 1.0, 1.9, and 1.5 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Mean attached tick counts were reported as 13.4, 2.2, 0.0, 0.0, 0.0, 2.8, 0.3, and 2.9 on days -7, 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of fleas was reported as 100.0%, 99.9%, 100.0%, 99.6%, 99.3%, 98.9%, and 98.7% on days 2, 7, 14, 21, 28, 35, and 42, respectively. Percent control of ticks was reported as 11.5%, 39.4%, -32.1%, 47.3%, 24.4%, -5.4%, and 12.6% on days 2, 7, 14, 21, 28, 35, and 42, respectively.

(4) **Conclusion: Partially Acceptable.** This study supports that 2517-RTI kills fleas on dogs for up to 42 days/6 weeks at the dose rate of 15.19 mg imidacloprid/kg body weight and 75.95 mg permethrin/kg body weight because efficacy in both G804S19- and G804S16-treated groups was over 90% through 42 days post application.

This study does not support that 2517-RTI kills lone star ticks at any dose rate because tick attachment in the placebo control group was too low. In dog and cat studies investigating efficacy against ticks, there should be ~25-

50% attachment (typically higher percent attachment is seen with dogs versus cats). General tick claims should be supported by studies demonstrating efficacy against Brown Dog ticks (*R. sanguineus*), American Dog ticks (*Dermacentor variabilis*), and Blacklegged ticks (*Ixodes scapularis*).

46978901. Assessment of the Efficacy of an Imidacloprid (10%) / Permethrin (50%) Spot-On against *Stomoxys calcitrans* on Dogs.

(1) non-GLP

(2) **Methods:** Eighteen dogs were screened for their attraction to biting stable flies (*Stomoxys calcitrans*). The two least attractive subjects were removed. The remaining 16 dogs were divided into 2 groups. Treatments were randomized; 8 dogs were treated and 8 were untreated. Treatment and untreated control groups were balanced with regard to sexes as well. Dogs weighed between 8 and 16 kg. The application rate was 0.1ml/kg body weight. Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **11.27 mg imidacloprid/kg body weight** (range of doses tested is 11.26-11.31 mg imidacloprid/kg body weight) and **56.36 mg permethrin/kg body weight** (range of doses tested is 56.30-56.55 mg permethrin/kg body weight) if the density assumption is correct.

Individual dogs were penned and exposed to biting stable flies. The adult flies were 14 days old and fasted from blood for three days and sucrose solution for one day prior to exposure. Each dog was exposed to 25 starved flies at each exposure period (day 1, 8, 18, 22 and 29) for 30 minutes. On day 18, only 20 flies were applied. Dogs were sedated during each exposure period. The number of alive, dead, and blood-fed flies was counted at each exposure period for treated dogs. Blood-fed fly counts included both dead/moribund as well as alive flies. Lack of blood-feeding success was indicative of repellency. Abbott's formula was used to calculate percent efficacy for the treatment group in terms of repellency:

$$\% \text{ Control} = [(X - Y) / X] (100)$$

Where: X = Mean number of blood-fed flies from control animals
Y = Mean number of blood-fed flies from treated animals

(3) **Results:**
Blood Feeding/Repellency: Percent efficacy was reported as 93.3%, 84.7%, 96.8%, and 82.5% on days 1, 8, 18, 22, and 29, respectively. The mean number of blood-fed stable flies in the untreated control group was reported as 12.1, 14.0, 11.6, 4.9, and 11.3 on days 1, 8, 18, 22, and 29, respectively, indicating an adequate level of blood feeding in the untreated control group.

Mortality: Mortality in the treatment group was reported as 86.0%, 94.5%, 30.0%, 25.7%, and 37.7% on days 1, 8, 18, 22, and 29, respectively, although it is unclear if dead and moribund flies were recorded separately or combined. Control mortality was unacceptably high on day 8 (17%) and day 22 (11%); and was acceptably low on all other challenge days.

(4) **Conclusion: Partially Acceptable.** This study supports that 2517-RTI repels stable flies on dogs for up to 22 days/3 weeks at the dose rate of 11.27 mg imidacloprid/kg body weight and 56.36 mg permethrin/kg body weight because percent efficacy (repellency) in the treatment group was over 90% through 22 days post application. Percent efficacy (repellency) declined to just 82.5% on day 29, which is too low for claims to be supported.

"Kills" claims are not supported by this study because mortality in the treatment group was well below 90% at all but one time point. The only time point where adequate mortality in the treatment group was observed (day 8) also had unacceptably high mortality in the untreated control group. It is also unacceptable to combine dead and moribund individuals when calculating mortality. Only dead individuals should be included in mortality calculations.

For claims against biting flies, testing should be conducted on 3 species: biting midge (*Culicoides* sp.), stable fly (*Stomoxys calcitrans*), and black fly (one of either a *Simulium* sp. or *Prosimulium* sp.). Since only stable fly data were included with this submission, claims against biting flies are not supported.

46978902. Assessment of the Efficacy of an Imidacloprid (10%) / Permethrin (50%) Spot-On against *Stomoxys calcitrans* on Dogs.

(1) non-GLP

(2) **Methods:** Twenty-four dogs were screened for their attraction to biting stable flies (*Stomoxys calcitrans*). The four least attractive subjects were removed. The remaining 20 dogs were divided into 2 groups. Treatments were randomized with 10 dogs treated and 10 untreated. Treatment and untreated control groups were balanced with regard to sexes as well. Dogs weighed between 8 and 16 kg. The application rate was 0.1ml/kg. Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation, the rates of imidacloprid and permethrin tested with this formulation are within the rates on the proposed product label. Note the mean doses tested are **11.28 mg imidacloprid/kg body weight** (range of doses tested is 11.26-11.32 mg imidacloprid/kg body weight) and **56.40 mg permethrin/kg body weight** (range of doses tested is 56.30-56.62 mg permethrin/kg body weight) if the density assumption is correct.

Individual dogs were penned and exposed to biting stable flies. The adult flies were 14 days old and fasted from blood for three days and sucrose solution for one day prior to exposure. Each dog was exposed to 25 starved flies at each exposure period (day 1, 8, 18, 22 and 29) for 30 minutes. Dogs were sedated during each exposure period. The number of alive, dead, and blood-fed flies was counted at each exposure period for treated dogs. Blood-fed fly counts included both dead/moribund as well as alive flies. Lack of blood-feeding success was indicative of repellency. Abbott's formula was used to calculate percent efficacy for the treatment group in terms of repellency:

$$\% \text{ Control} = [(X - Y) / X] (100)$$

Where: X = Mean number of blood-fed flies from control animals
Y = Mean number of blood-fed flies from treated animals

(3) **Results:**
Blood Feeding/Repellency: Percent efficacy was reported as 81.88%, 88.28%, 86.21%, 90.38%, and 81.71% on days 1, 8, 18, 22, and 29, respectively. The mean number of blood-fed stable flies in the untreated control group was reported as 15.1, 13.1, 12.9, 15.7, and 16.6 on days 1, 8, 18, 22, and 29, respectively, indicating an adequate level of blood feeding in the untreated control group.

Mortality: Mortality in the treatment group was reported as 76.27%, 73.55%, 75.32%, 71.68%, and 56.90% on days 1, 8, 18, 22, and 29, respectively, although it is unclear if dead and moribund flies were recorded separately or combined. Control mortality was acceptably low (≤10%) on all challenge days.

(4) **Conclusion: Unacceptable.** This study does not support that 2517-RTI repels stable flies on dogs at the dose rate of 11.28 mg imidacloprid/kg body weight and 56.40 mg permethrin/kg body weight. Although percent efficacy (repellency) in the treatment group briefly exceeded 90% on day 22, it was below 90% on days 1, 8, 18, and 29. Percent efficacy should be demonstrated through the treatment interval indicated on the product label for claims to be supported.

"Kills" claims are not supported by this study because mortality in the treatment group was well below 90% at all time points. It is also unacceptable to combine dead and moribund individuals when calculating mortality. Only dead individuals should be included in mortality calculations.

47109101. Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of K9 Advantix® for Flea and Tick Control on Dogs.

(1) non-GLP

(2) **Methods:** In this study, dogs weighing 38 – 68 lbs were treated on day 0 with an 8.8% imidacloprid and 44% permethrin combination product using the following dosing scheme: dogs 21-55 lbs - 2.5 ml product, and dogs over 55 lbs - 4 ml product. Dogs were then inoculated with 100 cat fleas (*Ctenocephalides felis*) on days 1, 6, 13, 20, and 27; and inoculated with 50 brown dog ticks (*Rhipicephalus sanguineus*) on days 0, 5, 12, 19, 26. Fleas and ticks were counted on days 2, 7, 14, 21, and 28. To test the water and shampoo resistance, dogs were immersed for 30 seconds on days 2, 9, 16, and 23, and dogs were shampooed on day 14. Eight dogs were included in Group 1 (treated + shampoo), 8 dogs were included in Group 2 (treated + water immersion), 4 dogs were included in Group 3-1 (untreated control + shampoo), and 4 dogs were included in Group 3-2 (untreated control + water immersion). Treated + shampooed dogs were compared against only the untreated control + shampoo dogs, and treated + water immersed dogs were only compared against untreated control + water immersed dogs. Abbott's formula was used to calculate percent efficacy for Groups 1 and 2:

$$\% \text{ Control} = [(X - Y) / X] (100)$$

Where: X = Geometric mean of fleas or ticks from control animals
Y = Geometric mean of fleas or ticks from treated animals

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation, the rates of imidacloprid and permethrin administered to dogs in Group 1 are within the rates on the proposed product label. Note the mean doses tested are **13.30 mg imidacloprid/kg body weight** (range of doses tested is 10.71-15.89 mg imidacloprid/kg body weight) and **66.50 mg permethrin/kg body weight** (range of doses tested is 53.54-79.44 mg permethrin/kg body weight) if the density assumption is correct.

Assuming the formulation density of the proposed product 2517-RTI is similar to that of the tested formulation, the rates of imidacloprid and permethrin administered to dogs in Group 2 are within the rates on the proposed product label. Note the mean doses tested are **13.23 mg imidacloprid/kg body weight** (range of doses tested is 10.11-15.60 mg imidacloprid/kg body weight) and **66.13 mg permethrin/kg body weight** (range of doses tested is 50.57-78.02 mg permethrin/kg body weight) if the density assumption is correct.

(3) **Results:** Percent efficacy figures for Groups 1 and 2 are summarized in Table 1 for brown dog ticks and in Table 2 for cat fleas below. Over 90% efficacy against both cat fleas and dog ticks was observed from days 2 through 28.

Table 1: Percent Efficacy against Brown Dog Ticks

Rhipicephalus sanguineus

Study Day	Group 1 (shampoo)	Group 2 (water immersion)
2	97.9%	100%
7	99.0%	100%
14	100%	98.4%
21	98.3%	100%
28	97.4%	97.9%

Table 2: Percent Efficacy against Cat Fleas

Ctenocephalides felis

Study Day	Group 1 (shampoo)	Group 2 (water immersion)
2	100%	100%
7	100%	100%
14	100%	99.7%
21	98.1%	95.1%
28	99.1%	92.5%

Mean flea counts in the untreated control + shampoo group (3-1) were reported as 64.8, 84.5, 72.3, 76.8, and 71.8 on days 2, 7, 14, 21, and 28, respectively, indicating an adequate level of flea infestation in the shampoo control group through 28 days. Mean flea counts in the untreated control + water immersion group (3-2) were reported as 67.3, 80.5, 81.8, 86.6, and 49.3 on days 2, 7, 14, 21, and 28, respectively, indicating an adequate level of flea infestation

in the water immersion control group on all count days except day 28. However, adequate flea pressure was seen in the shampoo control group on day 28 (mean of 71.8 ticks). Because of this, and because shampooing is considered to have a greater effect on spot-on product removal than water immersion, efficacy claims against fleas can be supported for up to 28 days if rinsing parameters are met.

Mean attached tick counts in the untreated control + shampoo group (3-1) were reported as 32.8, 31.3, 28.5, 29.3, and 23.3 on days 2, 7, 14, 21, and 28, respectively, indicating an adequate level of flea infestation in the shampoo control group through 28 days. Mean attached tick counts in the untreated control + water immersion group (3-2) were reported as 39.5, 42.3, 27.5, 35.3, and 22.0 on days 2, 7, 14, 21, and 28, respectively, indicating an adequate level of flea infestation in the water immersion control group through 28 days.

(4) **Conclusion: Partially Acceptable.** This study supports that 2517-RTI kills fleas and brown dog ticks for up to 28 days/4 weeks/1 month at the dose rate of 13.30 mg imidacloprid/kg body weight and 66.50 mg permethrin/kg body weight, as efficacy in treated groups was over 90% through 28 days post application. Furthermore, this study supports that the subject product maintains efficacy against fleas and brown dog ticks after swimming/exposure to rain/water immersion for 4 weeks/1 month at the aforementioned dose rates. Claims that 2517-RTI withstands shampooing/bathing and maintains efficacy against fleas and brown dog ticks are not supported at the aforementioned dose rates. Animals undergoing shampoo/bathing resistant tests should be shampooed with a non-medicated shampoo and then rinsed for at least 5 minutes using a minimum of a 3.0 gallon per minute showerhead. The shampoo/rinsing procedures in MRID 47109101 were inadequately detailed for these parameters to be determined. Moreover, although the test substance contains the same amount of imidacloprid and permethrin as the subject product, the inert/other ingredients differ; the extent of these formulation differences is not known. Because inert/other ingredients may play such a large role in spot-on product characteristics like shampoo resistance, efficacy testing to support these type of claims should be conducted with the formulated product itself.

Tick claims cannot be supported by this study alone, as efficacy should be demonstrated against Brown Dog ticks (*R. sanguineus*), American Dog ticks (*Dermacentor variabilis*), and Blacklegged ticks (*Ixodes scapularis*). This study may be combined with other studies to support a tick claim, however.

47298201. Addendum 1 to: Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of K9 Advantix® for Flea and Tick Control on Dogs.

(1) non-GLP

(2) **Conclusion: Supplemental.** This MRID contains the protocol and raw data for the study described in MRID 47109101.

43396409. Study Report for the Efficacy Evaluation on ECTO Flea and Tick Insecticide with IGR for Fleas, Ticks, and Mosquitoes.

(1) GLP

(2) **Methods:** Six dogs (3 dogs < 33 lb, and 3 dogs > 33 lb) were treated with a 45% permethrin and 5% pyriproxyfen dermal pesticide. On day 0, dogs under 33 lb were treated with 1.5 ml product (0.05 fl. oz product) between the shoulder blades, and dogs over 33 lb were treated with 1.5 ml product between the shoulder blades and 1.5 ml product directly above the tail head (3 ml product per animal, 0.10 fl. oz. per animal). Similarly, six dogs were utilized as an untreated control group. Dogs were infested with 100 adult fleas and 50 adult brown dog ticks on days 0, 10, 17, and 24. Hand body counts were made on days 1-3, 11-3, 18-20, and 25-27 to determine product efficacy. Ovicidal tests were also performed on these animals by infesting them with 150-200 adult fleas on days 45 and 90. Four days after these infestations, 100 flea ova were collected and observed through adult emergence to determine ovicidal efficacy.

On days 4 and 27 post treatment, deer tick efficacy was evaluated by taking fur samples from two dogs per treatment group (4 dogs total, 1 > 33 lb and 1 < 33 lb) from areas of the animal which were not directly treated. Clipped fur was then placed into a test tube and each test tube was inoculated with an unknown number of deer tick nymphs (10

or 18 – resolution is unclear). Counts of live and dead deer ticks were made at 24 and 48 h post exposure to the fur.

On days 5, 14, 21, and 28, two dogs from each treatment were sedated and placed into Gerberg type cages with 50 unfed adult female *Aedes aegypti* mosquitoes. The number of landings in five minutes was recorded immediately after placement, and two hours later the number of live and dead mosquitoes were counted. Efficacy calculations were made as a function of insects on the untreated control animals.

(3) **Results:** Control of adult fleas was generally over 90% through day 20 on both weight groups, however beginning on day 25 efficacy was under 90% of fleas for both weight groups. Efficacy against brown dog ticks was less than 90% for both weight groups 3 days after treatment, but on days 11-20 efficacy was over 90% for both groups. During the brown dog tick counts on days 25-27, efficacy was under 90% on the under 33 lb group, but efficacy was greater than 90% on the over 33 lb group. However, numbers of brown dog ticks on the control dogs were low, usually less than 10 per animal. No live deer ticks were found in vials with insecticide treated hair, while untreated vials had an average of 12 live deer ticks per vial. Mosquito landings were reduced by 56% and blood feeding was reduced by 100%. Percent mosquito mortality was 97%.

(4) **Conclusion: Unacceptable.** Sample size in the deer tick and mosquito tests was not adequate with only two individual dogs tested. The rates utilized in this study are higher than the labeled rates for the product this study is intended to support, and the tested product is different than the labeled product. Moreover, inoculations were made through 24 days post treatment for both ticks species and for month long control claims, the final infestation should be at 28 days post treatment. Furthermore, percent efficacy against fleas and adult brown dog ticks was less than 90% at the last timepoint (27 days post treatment) – too low for efficacy claims to be supported.

43396410. Study Report for the Efficacy Evaluation on ECTO Flea and Tick Insecticide with IGR for Fleas, Ticks, and Mosquitoes.

(1) GLP

(2) **Methods:** Six dogs (3 dogs < 33 lb, and 3 dogs > 33 lb) were treated with a 45% permethrin and 5% pyriproxyfen dermal pesticide. On day 0, dogs under 33 lb were treated with 1.5 ml product (0.05 fl. oz product) between the shoulder blades, and dogs over 33 lb were treated with 1.5 ml product between the shoulder blades and 1.5 ml product directly above the tail head (3 ml product per animal, 0.10 fl. oz. per animal). Four dogs, two in each weight class above, were used as a control group. Two days prior to treatment, dogs were infested with 50 adult brown dog ticks, 50 adult American dog ticks, and 100 adult fleas. Dogs were also infested at 6, 13, 20, and 27 days after treatment with the insecticide. Flea and tick numbers on each dog were counted at 2, 9, 16, 23, and 30 days after treatment (3 days after infestations). Ticks were counted by parting the hair and counting live ticks, and flea counts were performed by combing the dogs and counting the number of live fleas removed.

(3) **Results:** The number of fleas counted on treated dogs weighing more than 33 lbs was reduced by over 90% through 23 days post treatment when compared to the number of fleas on untreated dogs. At 30 days post, flea numbers on treated dogs weighing more than 33 lbs were reduced by 77% compared to the number on untreated dogs. Flea numbers on treated dogs weighing less than 33 lbs were reduced by over 90% though 16 days post treatment when compared to the number of fleas on untreated dogs. On days 23 and 30, the reduction in flea numbers on the treated dogs weighing less than 33 lbs was only 72% and 51%, respectively, when compared to flea numbers on untreated dogs. The number of brown dog ticks was over 90% lower on treated dogs over 33 lb than on untreated dogs on days 9, 16, 23, and 30 post treatment, however, the number of brown dog ticks was only reduced by 64% at 2 days post treatment. On treated dogs under 33 lb, the number of brown dog ticks was reduced by 70% at two days post treatment, over 90% on days 9, 16, and 23 after treatment, and 72% at 30 days after treatment when compared to the control group. The number of American dog ticks on treated dogs weighing more than 33 lb was reduced by 49% two days post application, and over 90% on days 9, 16, 23, and 30 post application when compared to untreated dogs. However, on treated dogs weighing less than 33 lb, the number of American dog ticks were reduced 40% on day two, 99-100% on days 9 and 16, 82% on day 23, and 65% on day 30 post application when compared to untreated dogs.

(4) **Conclusion: Unacceptable.** The rates utilized in this study are higher than the labeled rates for the product this

study is intended to support, and the tested product is different than the labeled product. In addition, only four dogs were used in the control group. A minimum of six dogs should be used in all treatment groups. Furthermore, percent efficacy against fleas, brown dog ticks, and American dog ticks did not remain ≥90% at 30 days post treatment. Percent efficacy should be demonstrated through the treatment interval indicated on the product label for claims to be supported.

45086801. Study Report for the Efficacy Evaluation on ECTO Flea and Tick Insecticide with IGR for Fleas, Ticks, and Mosquitoes.

(1) non-GLP

(2) **Methods/Results:** The first two studies evaluated the efficacy of dip and shampoo treatments on cats. These studies tested pyriproxyfen against adult cat fleas and eggs. **These studies are unacceptable and do not support public health pest claims for the proposed product because only 5 cats were tested per study, too few to provide statistically meaningful results. Moreover, efficacy studies investigating dip and shampoo formulations should not be relied upon to support spot-on products such as 2517-RTI. More importantly, efficacy data from cat studies should not be relied upon to support claims for a product that is applied to dogs.**

The third study examined egg mortality by placing 50 fleas in a 10 mg vial treated with 0.25µg/cm^2 pyriproxyfen for 24 hours. Fleas were then removed, and placed on one of 2 cats. Forty-six hours after treatment, fleas began to lay eggs containing yolk and 70 hours after treatment, flea eggs were normal. Researchers in this study did not allow eggs to hatch, rather they evaluated the eggs through dissection. Using a microscope, eggs were carefully cut open and the inside contents were then evaluated for egg viability. Pyriproxyfen at low doses did not prevent the laying of eggs and although egg viability was evaluated through dissection, researchers did not follow any eggs for enough time to determine if any were able to develop into viable offspring. **Witnessing the egg hatch is needed to make a true determination of egg viability, therefore, this study is unacceptable. Furthermore, flea exposure to pyriproxyfen residues on glass vials is not an adequate simulation of real-world exposure for spot-on formulations. Efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals. More importantly, efficacy data from cat studies should not be relied upon to support claims for a product that is applied to dogs.**

The fourth study was an in-vitro study in which, flea eggs were exposed to 9 cm diameter (63.6 cm^2 area) filter paper treated with pyriproxyfen at the rate of 1.1 µg/cm^2. Filter paper on average weighed 460 mg (the converted rate of treatment was thus 152 mg/1kg of pyriproxyfen). Control papers were treated with alcohol. Eggs were divided into 5 groups of 20 replicates and were exposed for varying times depending on the age of the egg. If the egg was between 0-4 hours old, it would receive a treatment of either 1 minute, 10 minutes, or 60 minutes. A 24 hour old egg would be exposed for a time of 1 minute, 30 minutes, or 60 minutes, and a 48 hour old egg would receive a treatment for 1 minute, 30 minutes, or 60 minutes. After the assigned exposure time, eggs were transferred to a clean filter paper with a larval feeding diet. After 5 days, hatch percentage was determined and after 4 weeks, the percent of eggs that developed into adults was determined. **The study is also unacceptable for this product as the tested rate of pyriproxyfen (152 mg/1 kg) is higher than the intended label rate (0.36-1.30 mg/kg). In addition, efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals.**

The next study was also an in-vitro study that exposed flea eggs to pieces of dog hair (obtained from a groomer). In the non-negative control groups, each piece of dog hair received 1 mL treated with 0.125 % pyriproxyfen, while the control hair pieces were treated with isopropyl alcohol. Each piece of hair was approximately 460 mg which equated to a treatment rate of roughly 152 mg/1 kg. After treatment, 100 eggs were divided into 5 groups and were exposed to pieces of hair for 1 minute, 10 minutes, 30 minutes, or 60 minutes. After exposure, eggs were transferred to a clean holding area and were observed to determine percent hatch and eventually percent adult emergence. This study was replicated 1 day, 2 months, 4 months, and 6 months after treatment. **The study is also unacceptable for this product as the tested rate of pyriproxyfen (152 mg/1 kg) is higher than the intended label rate (0.36-1.30 mg/kg). In addition, efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals.**

The next study was also an in-vitro test of adult fleas on treated filter paper. Groups of 20 adult fleas were collected from breathing on 7-10 day old cocoons. Each group was separated into 0.5 liter glass canning jars containing either pyriproxyfen treated or acetone treated filter paper and held for 10 days. Filter papers were 7 cm in diameter, but the weight of each paper was not given. Pyriproxyfen-treated papers were treated at the rate of 1.1 $\mu g/cm^2$. If we assume each filter paper weighs 460 mg (as in the other filter paper studies within this MRID), the converted application rate is thus 152 mg pyriproxyfen/1kg. Mortality was evaluated and compared to control jars daily. Ninety percent mortality was reached after forced flea exposure for 7 days. **However, the study is also unacceptable for this product as the tested rate of pyriproxyfen (152 mg/1 kg) is higher than the intended label rate (0.36-1.30 mg/kg). Also, ninety percent mortality should be demonstrated by the fourth day of forced exposure. This did not occur until 7 days post-exposure. In addition, efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals.**

The next study (in-vitro) tested 5 day old adult fleas. Fleas were placed in 5 cm diameter cages and fed blood using an "artificial dog" feeding system. Cages were lined with dog hair treated with pyriproxyfen at a rate of 352 µg/gram of dog hair. This is equivalent to 352 mg/1 kg. Hair in the control cages were treated with 5 ml of acetone. Hair dried for 2 hours in a fume hood before placement in the 5 replication cages. One hundred adult fleas were placed in each cage. Fleas rested on dog hair in close proximity to a parafilm membrane where they were fed warm bovine blood. Cages were checked daily for mortality of dead fleas for 9 days. Mortality of fleas reached 90% 7 days after treatment. **However, the study is also unacceptable for this product as the tested rate of pyriproxyfen (352 mg/1 kg) is higher than the intended label rate (0.36-1.30 mg/kg). Also, ninety percent mortality should be demonstrated by the fourth day of forced exposure. This did not occur until 7 days post-exposure. In addition, efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals.**

Flea eggs of different ages were exposed in-vitro to filter paper treated with 1.1 µg of pyriproxyfen/cm^2. Filter papers were 9 cm in diameter, but the weight of each paper was not given. If we assume each filter paper weighs 460 mg (as in the other filter paper studies within this MRID), the converted application rate is thus 152 mg pyriproxyfen/1kg. The three groups of eggs were placed on the treated or control papers at 0-4 hours, 24 hours, and 48 hours. Each subgroup was removed at their designated time interval and placed in a clean container with larval diet. Eggs were observed and hatch rate was determined for 5 days post removal from treatment. For eggs aged 24 hours or less, a 2 hour exposure of pyriproxyfen was enough to limit percent hatch to a high of 9%, though 22% hatch was observed with 48 hour-old eggs exposed to pyriproxyfen for 2 hours. **However, the study is also unacceptable for this product as the tested rate of pyriproxyfen (152 mg/1 kg) is higher than the intended label rate (0.36-1.30 mg/kg). Also, ninety percent mortality should be demonstrated by the fourth day of forced exposure. This did not occur until 7 days post-exposure. In addition, efficacy testing of spot-on products should be conducted with spot-on formulations applied to the appropriate test animals.**

(3) **Conclusion: Unacceptable.** This MRID consisted of 8 studies with varying methods. Six out of the 8 studies were in-vitro studies instead of in-vivo. The two in-vivo studies had insufficient replication to support meaningful statistical results, while the in-vitro studies were conducted with application rates far greater than those on the proposed label for 2517-RTI. More importantly, efficacy data from cat studies should not be relied upon to support claims for a product that is applied to dogs. The data generated from these studies, for reasons described above, do not support "kills adult fleas, flea eggs, flea larvae, or flea pupae" or any flea IGR-based claims on the label of the proposed product.

43679609. Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Dogs.

(1) GLP

(2) **Methods:** To test for efficacy against fleas, a 10% imidacloprid spot-on product was applied to 32 dogs (8 dogs in each treatment group) at the following rates: 0, 3.75 mg, 7.5 mg, and 10.0 mg imidacloprid/kg body weight. Dogs in the control group (0% imidacloprid) were treated with a blank vehicle. Dogs were infested with approximately

100 adult fleas on days -1, 6, 13, 20, 27, and 33. Fleas were visually counted on days 1, 7, 14, 21, and 28, and on day 34 fleas were combed out of the fur and counted.

(3) **Results:** All imidacloprid treatments killed over 90% of fleas through 34 days post application. Flea survival on control animals was adequate to evaluate efficacy of the imidacloprid treatment.

(4) **Conclusion: Acceptable.** This study supports efficacy claims of kills fleas for up to 34 days (or up to 1 month) at a rate of 3.75 mg imidacloprid/kg body weight for a dog spot-on product.

43679610. Efficacy Confirmation of NTN 33893 (Imidacloprid) Solution Applied Dermally for Control of Fleas on Dogs.

(1) non-GLP

(2) **Methods:** Thirty-seven adult dogs of various breeds and hair lengths were initially selected for the study. On day -2, all 37 dogs were infested with 100 unfed adult fleas. Fleas were combed out, counted, and removed on day -1. Thirty dogs (18 female, 12 male) were chosen to participate in the study on day -1 based on their attractiveness to fleas. Ten dogs were treated with 8.5 mg imidacloprid/kg body weight (8.5% imidacloprid product at 0.1 mL/kg body weight), ten were treated with 10 mg imidacloprid/kg body weight (5.0% imidacloprid product at 0.2 mL/kg body weight) and ten dogs were treated with a placebo control. All treatments were applied directly to the skin. Dogs were infested with 100 adult fleas each on days 6, 13, 20, 27, and 34 (note that the study does not indicate that fleas were inoculated on day -1 or 0). Fleas were counted visually on days 1, 7, 14, 21, and 28, and were combed out and counted on days 35 and 42.

(3) **Results:** Both imidacloprid treatments killed over 90% of fleas through 35 days post treatment. Flea numbers in the control treatment were adequate to evaluate efficacy. Note that the number of fleas per animal was counted on day 1, but the study does not indicate that animals were inoculated with fleas after the comb out on day -1 but before this count. However, 494 total fleas were present on the control animals (49.4 fleas per dog) on day 1 indicating that fleas were inoculated before the day 1 count.

(4) **Conclusion: Partially Acceptable.** This study supports claims of kills fleas for up to 35 days (1 month) post application at a dose of 8.5 mg imidacloprid/kg body weight.

47190401. A Controlled Randomised Study to Evaluate the Efficacy of Advantage Against a Natural Infestation of Dog Lice (*Trichodectes canis*) Following a Single Topical Administration to Adult Mixed Breed Dogs.

(1) non-GLP

(2) **Extraneous.** Efficacy data on dog lice are not required to be submitted to the Agency therefore the study will not be reviewed here.

IV. EXECUTIVE DATA SUMMARY:

(A) The cited data reviewed in this DER support a number of efficacy claims against various arthropod pests of public health importance for the proposed product 2517-RTI. Due to the large number of studies submitted with this action, overall conclusions are broken down by pest below:

Fleas:
The proposed product 2517-RTI kills fleas on dogs at the rate of 3.75 mg imidacloprid/kg body weight or **42.4 mg product/kg body weight for up to 34 days/4 weeks/1 month**, assuming equivalent densities.

The proposed product 2517-RTI kills fleas on dogs at the rate of 8.5 mg imidacloprid/kg body weight or **96.2 mg product/kg body weight for up to 35 days/5 weeks/1 month**, assuming equivalent densities.

The proposed product 2517-RTI kills fleas on dogs at the rate of 15.19 mg imidacloprid/kg body weight or **171.9 mg product/kg body weight for up to 42 days/6 weeks/1 month**, assuming equivalent densities.

The proposed product 2517-RTI kills fleas on dogs after swimming/exposure to rain/water immersion at the rate of 13.3 mg imidacloprid/kg body weight or **150.5 mg product/kg body weight for up to 4 weeks/1 month**, assuming equivalent densities.

Claims that 2517-RTI withstands shampooing/bathing and maintains efficacy against fleas are not supported. Animals undergoing shampoo/bathing resistant tests should be shampooed with a non-medicated shampoo and then rinsed for at least 5 minutes using a minimum of a 3.0 gallon per minute showerhead. In addition, because inert/other ingredients may play such a large role in spot-on product characteristics like shampoo resistance, efficacy testing to support these type of claims should be conducted with the formulated product itself.

No IGR claims against fleas are supported. No speed of kill claims against fleas are supported.

Stable Flies: The proposed product 2517-RTI repels stable flies on dogs at the rate of 11.27 mg imidacloprid/kg body weight or **127.5 mg product/kg body weight for up to 22 days/3 weeks**, assuming equivalent densities. For claims against biting flies, testing should be conducted on 3 species: biting midge (*Culicoides* sp.), stable fly (*Stomoxys calcitrans*), and black fly (one of either a *Simulium* sp. or *Prosimulium* sp.). Since only stable fly data were included with this submission, claims against biting flies are not supported.

Ticks: No claims against ticks are supported. For dog products, efficacy should be demonstrated against Brown Dog ticks (*Rhipicephalus. sanguineus*), American Dog ticks (*Dermacentor variabilis*), and Blacklegged ticks (*Ixodes scapularis*). Of these 3 species, only data on Brown Dog ticks and American Dog ticks were submitted to support efficacy claims against ticks. Claims against only Brown Dog ticks and/or American Dog ticks cannot be supported because consumers cannot readily distinguish these ticks from other ticks.

Mosquitoes: No claims against mosquitoes are supported.

V. LABEL RECOMMENDATIONS:

(1) The following changes in the Directions for Use are suggested:

On page 10/14, under Product Information, the first paragraph should be changed to read: "The successive feeding activity of fleas on dogs may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with this product [or ABN] kills fleas which may cause flea allergy dermatitis (FAD)."

On page 10/14, under Product Information, the second paragraph should be deleted. Speed of kill and IGR claims are not supported.

On page 10/14, under Product Information, the third paragraph should be changed to read: "This product [or ABN] is waterproof and remains effective following swimming or exposure to rain." Claims that the product is efficacious after bathing/shampooing and exposure to sunlight are not supported by any efficacy data.

On page 11/14, under Product Information, the fourth paragraph should be changed to read: "Monthly treatments are required for optimal control and prevention of fleas." Tick claims are not supported.

On page 13/14, the following pests should be removed from the graphic because they are not supported by efficacy data: flea eggs, flea larvae, flea pupae, ticks, deer ticks, brown dog ticks, lone star ticks, American dog ticks, mosquitoes, biting flies. Adult fleas, fleas, lice, biting lice, and chewing lice may remain.

On page 13/14, the clock graphic should be deleted because speed of kill claims are not supported.

On page 13/14, the flea eggs and flea larvae graphics should be deleted because IGR claims and claims against flea life stages other than adults are not supported. These two graphics appear immediately to the left of the waterproof

graphic.

The flea life cycle graphic at the top left of page 14/14 should be removed because claims against flea life stages other than adults are not supported by efficacy data.

(2) The following marketing claims are acceptable:

[Kills fleas]
[Kills fleas on dogs]
[Active against fleas]
[Treats Fleas]
[Prevents Fleas]
[Controls against [irritating] flea bites]
[[Brand Name] Offers protection against fleas]
[Prevents and treats flea[s] [infestations]]
[Controls existing infestations by killing adult fleas]
[Controls existing flea infestation by killing adult fleas]
[For the prevention and treatment of Flea Infestations]
[Kills fleas even if your dog gets wet]
[May be used year-round for control of fleas]
[Controls fleas, which can serve as an intermediate tapeworm host]
[One treatment prevents further flea infestations for [(a month) (four (4) weeks)]]
[Prevents further flea infestation for [[four][4] weeks][1 month] with one treatment]
[Prevents further flea infestation for [[four][4] weeks][1 month] with one application]
[[Brand Name] Prevents further flea infestation for [[four][4] weeks][1 month]]
[Once per month topical flea treatment for dogs]
[Once-a-month topical treatment for fleas on dogs]
[Prevents flea re-infestations for 30 days [1 month]]
[Prevents further flea infestations on dogs for 30 days [1 month]]
[Apply monthly [to control and prevent fleas]]
[Monthly topical flea treatment for dogs]
[Monthly treatments are required for optimal control and prevention of fleas]
[The Only Flea Protection You Need For Your Dog[s] When Applied Monthly!]
[[Once per month][Monthly] topical flea treatment for dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Once per month][Monthly] topical flea treatment for dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Once-a-month topical treatment for fleas on dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Kills fleas on dogs and puppies 7 weeks or older and 4-10 or 11-20 or 21-55 or over 55 pounds [lbs]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs]
[Flea control for puppies and dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Flea control for puppies and dog 7 weeks [of age] or older] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs over 7 weeks [old][of age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[[Brand Name][This product] is for the treatment and prevention of fleas on dogs 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Kills fleas that may cause flea allergy dermatitis, flea bite anemia, and tapeworm infestation]
[Kills Lice]
[Kills [(biting)(chewing) lice]

[Controls existing [(biting)(chewing)] lice infestations]
[Kills [(biting)(chewing)] lice and prevents further infestations]
[Provides effective control of [(biting)(chewing) lice [infestations]]
[Treats, prevents and controls [(biting)(chewing) lice [infestations]]
[For treatment and prevention of [(biting)(chewing) lice [infestations]]
[For treatment and prevention of infestations with [(biting) (chewing)] lice]
[Brand Name] contains [an][the] [insect growth regulator] [IGR] [, Pyriproxyfen] [, in addition to Imidacloprid, and permethrin]
[This product [or ABN] contains [Imidacloprid], [permethrin] and [an/the] [insect growth regulator] [IGR] [Pyriproxyfen]
[(Begins/Starts) working through contact]
[For use on dogs and puppies 7 weeks of age and older.]
[Apply to [dogs and] puppies over 7 weeks old and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Apply to [dogs and] puppies 7 weeks or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Formulated for Dogs and Puppies Over 7 Weeks [Old][of Age] and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Formulated for Dogs and Puppies 7 Weeks [of Age] or Older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Dogs and Puppies over 7 weeks [old][of age] [or] 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Can be used on puppies over 7 weeks [old][of age] [or] 7 weeks [of age] or older and 4-10 or 11-20 or 21-55 or over 55 lbs[pounds]] {weight range depends upon appropriate ml/fl oz package size}
[Waterproof]
[Remains effective even after the dog swims]
[Once a month treatment]
[Apply once every [4 weeks] [month] [30 days]!]
[4 Week Dose!] [1 Month Dose!] [30 Day Dose!]
[Once a month topical flea treatment for dogs 7 weeks of age or older]
[A single topical application remains effective for [(a month) (four (4) weeks)]]
From the Frequency of Application section in the DFU on page 10/14:
[Use [Brand Name {or} this product] monthly for control of flea[s] [infestations]:]
[If your dog is at high risk for flea reinfestation [, or in a highly infested environment], apply monthly.]
[Apply monthly for flea control.]

(3) The following marketing claims are unacceptable:

[Repels and kills Fleas]
[Repels biting flies]
[Repels and kills fleas before they lay eggs]
[Prevents reinfestations by killing adult fleas before they lay eggs]
[Repels, and inhibits blood-feeding by biting flies]
[Repels, and prevents blood-feeding by biting flies]
[[(prevents)(inhibits)] blood-feeding by biting flies]
[Repels [(annoying)(bothersome)(nuisance)] biting flies]
[Inhibits [(annoying)(bothersome)(nuisance)] biting flies]
[Kills reinfesting fleas within 2 hours [and protects against further infestation]]
[Kills fleas within 12 hours [of application][on dogs]]
[Kills fleas within 12 hours, continues to kill for 4 weeks]
[Kills fleas on dogs within 12 hours and continues to prevent infestations for [(a month) (four (4) weeks)]]
[Kills fleas within 12 hours on dogs [and prevents further infestations for [up to] [[4][four] weeks][[1][one][a] month]]
[Apply monthly [for effective flea control]]
[Kills fleas, which may be a source of flea allergy dermatitis within 12 hours]

[[Use of Brand Name][Use of this product] kills fleas and may reduce incidence of flea bite hypersensitivity] [and][or] [flea allergy dermatitis] [FAD]]
[[Use of Brand Name][Use of this product] kills fleas and may reduce incidence of [flea bite hypersensitivity] [and][or] flea allergy dermatitis [FAD]]
[Monthly treatment [with Brand Name][with this product] kills fleas and may reduce incidence of [flea bite hypersensitivity] [and][or] flea allergy dermatitis [FAD]]
[Monthly treatment [with Brand Name][with this product] kills fleas and may reduce incidence of flea bite hypersensitivity [and][or] [flea allergy dermatitis] [FAD]]
[Treatment with this product [or ABN] rapidly kills fleas and may reduce the incidence of Flea Allergic Dermatitis [FAD]]
[[Brand Name][This product] kills fleas and may reduce the incidence of a hypersensitivity skin disorder called flea allergy dermatitis (FAD), which may be caused by the feeding activity of fleas on dogs.]
[Treats Ticks]
[Prevents Ticks]
[Repels and kills Ticks]
[Repels and kills ticks including Deer ticks (vector of Lyme disease), American dog ticks (vector of Rocky Mountain spotted fever), Brown dog ticks (vector of Ehrlichiosis), and Lone Star ticks (vector of Ehrlichiosis), for up to four weeks]
[Repels and kills Mosquitos]
[Repels and kills mosquitoes [for up to four weeks]
[Repels and kills mosquitoes often before they have a chance to take a blood meal]
[(Prevents blood-feeding by) (kills and repels)] mosquitoes]
[Kills flea eggs]
[Controls existing flea eggs]
[Prevents flea eggs from hatching]
[Prevents flea eggs from developing into [biting] adult fleas]REP
[Prevents the development of flea eggs into [biting] adult fleas]
[[Brand Name][This product] contains Pyriproxyfen [PPF] [an insect growth regulator (IGR)] to kill flea eggs [and protect against reinfestation]]
[Prevents flea eggs [and flea larvae] from developing into [(biting)(adult)] fleas]
[Prevents development of fleas, flea eggs, pupae and larvae [for (a month)(four (4) weeks)]]
[Kills [flea eggs and] flea larvae]
[Kills flea eggs and flea larvae for up to four [4] weeks][1 month]]
[Controls existing flea eggs and fleas and prevents future infestations for 30 days [1 month]]
[Monthly treatment controls existing flea eggs and fleas and prevents future infestations]
[Kills multi-stages of fleas]
[Kills multiple flea life stages]
[Breaks the flea life cycle]
[Effectively breaks the flea life cycle]
[Targets multi-stages of flea lifecycle]
[Controls multi-stages of flea lifecycle]
[Repels and kills all [life] stages of fleas]
[Prevents development of all flea stages [for (a month)(four (4) weeks)]]
[Provides multi-stage flea control]
[Prevents multi-stages of the flea life cycle from developing]
[Effectively targets all [life] stages of [flea] and [ticks]]
[Kills fleas before eggs can be laid]
[Treats ticks, fleas [and mosquitoes]]
[Prevents ticks, fleas [and mosquitoes]]
[Repels and kills ticks, fleas [and mosquitoes]]
[Flea Adulticide, larvicide and ovicide]
[[Brand Name][This product] is a flea ovicide, larvicide, and adulticide]
[Kills flea eggs, larvae, and [adult] fleas]
[Kills [adult] fleas, flea eggs, and flea larvae]
[Kills [adult] fleas, flea eggs and flea larvae for up to four [4] weeks][1 month]]

[Kills [adult] fleas, larvae, and eggs [, providing three-way protection]]
[3-way flea protection kills adults, larvae and eggs]
[3-way flea protection ([kills] [controls] adults, larvae, and eggs)]
[5-way protection (against fleas, ticks, biting flies, mosquitoes, and lice)]
[Topical prevention and treatment of ticks, fleas, mosquitoes, biting flies, and lice for monthly use.]
[This product [or ABN] is indicated for the prevention and treatment of fleas, ticks, biting flies, mosquitoes, and lice on dogs 7 weeks of age and older]
[Remains effective after bathing and/or swimming]
[Remains effective following swimming and/or shampooing]
[Remains effective after exposure to rain or sunlight]
[Remains effective, even after [bathing,][shampooing,] water immersion, or exposure to [sunlight] [and][or] rain]

From the Frequency of Application section in the DFU on page 10/14:
[[Studies show that] [Brand Name {or} This product] kills fleas within 12 hours of application and [lasts {or} protects] [for [up to] [[four][4] weeks][30 days][one month].]
[[Brand Name {or} This product] kills reinfesting fleas within [2][two] hours][two hours] and prevents further infestations of fleas [for [up to] [[four][4] weeks][30 days][one month]].]
[[Brand Name {or} This product] [targets multiple flea life stages] [and] [kills flea eggs and larvae before they develop into biting adults].]
[[Brand Name {or} This product] breaks the flea life cycle by killing flea eggs, flea larvae, and adult fleas.]
[[Brand Name {or} This product] is waterproof and remains effective, even after bathing**, swimming, or exposure to sunlight [and][or] [rain].] [Allow treated area to dry thoroughly.]

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product or "extraneous:"

44256902
46978902
43396409
43396410
45086801
47190401

(5) Note to reviewer/PM:

For claims against biting flies, testing should be conducted on 3 species: biting midge (*Culicoides* sp.), stable fly (*Stomoxys calcitrans*), and black fly (one of either a *Simulium* sp. or *Prosimulium* sp.). Since only stable fly data were included with this submission, claims against biting flies are not supported.

MRID 46978901 supports that 2517-RTI repels stable flies on dogs for up to 22 days/3 weeks at the dose rate of 11.27 mg imidacloprid/kg body weight and 56.36 mg permethrin/kg body weight. However, efficacy was not demonstrated for the full treatment interval (30 days/1 month) on the proposed label.

The Agency prefers that spot-on studies intended to support efficacy claims against public health pests be conducted using the lowest labeled dose rate for each animal (e.g. titrated doses). In several of the studies reviewed in this DER, animals were treated with the dose corresponding to labeled weight range in which each animal fell. In these cases, animals were dosed per label DFU, but not necessarily with the lowest labeled (most conservative) dose rate.

This review only addresses efficacy claims in the context of supporting efficacy data. Marketing claims on the proposed label not addressed in this DER are not considered to be efficacy claims.

me - to delta matrix

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

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DATA MATRIX

Date: February 29, 2008	EPA Reg No./File Symbol: 11556-141, 11556-143 11556-142, 11556-144	Page 9 of 11
Bayer Healthcare LLC, Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	Product: K9 Advantix® Plus 10 K9 Advantix® Plus 20 K9 Advantix® Plus 55 K9 Advantix® Plus 100	Ingredient: Imidacloprid, CAS = 138261-41-3 Permethrin, CAS = 52645-53-1 Pyriproxyfen, CAS = 95737-68-1

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note: Report Number	Note: Description
810.3300 (95-9)	Efficacy	45563011	11556	OWN	Report No. 75400 (Advantix)	Fleas and Brown Dog Ticks
		45573501	11556	OWN	Report No. 75401 (Advantix)	Fleas and Lone Star Ticks
		43679609	11556	OWN	Report No. 74572 (Advantage)	Dogs
		43679610	11556	OWN	Report No. 74541 (Advantage)	Dogs
		44256901	11556	OWN	Report No. 74800 (Advantage)	Speed of flea kill
		44256902	11556	OWN	Report No. 47828 (Advantage)	Larvicidal efficacy
		44256903	11556	OWN	Report No. 74792 (Advantage)	Effects of shampooing
		46978901	11556	OWN	Report No. 75863	Biting Flies
		46978902	11556	OWN	Report No. 75864	Biting Flies
		43396409	67505	PAY	Report No. F701R10	Permethrin
		43396410	67505	PAY	Report No. F701R11	Permethrin
		45086801	1021	PER	MGK Report No. OT018-94	Pyriproxyfen
		45086801	1021	PER	MGK Report No. OT016-93	Pyriproxyfen
		45086804	1021	PER	MGK Report No. OT006-96	Pyriproxyfen
		47109101	11556	OWN	Report No. 75867	Waterproof
		47298201	11556	OWN	Report No. 75867-1	Waterproof – Protocol & Raw Data
		47190401	11556	OWN	Report No. 75950 (Advantage)	Lice
Plant Protection, Section 158.540						
122-2	Aquatic plant growth					N.A.
123-2	Aquatic plant growth					N.A.
Non-Target Insects, Section 158.590						
141-1	Honey bee acute contact					N.A.
141-2	Honey bee residue on foliage					N.A.

Pages 45-70 Inert ingredient information may be entitled to confidential treatment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

FEE

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

DP Barcode No.: D436234 File Symbol No.: 2517-RTI Decision No.: 521126
PC Codes: 109701,129032,129099 Company Name: Sergeant's Pet Care Products, Inc.
Food Use: No Action Code: R315 Product Name: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze on for Dogs

DATE OUT: April 19, 2017

SUBJECT: End-Use Product Chemistry Review
Product Name: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze on for Dogs

FROM: Bruce F. Kitchens, Chemist
Product Chemistry Team
Chemistry, Inerts and Toxicology Assessment Branch/RD (7505P)

Bruce F. Kitchens 4/19/17

TO: RM #04, Laura Bacon/Autumn Metzger
Invertebrate and Vertebrate Branch 1
Registration Division (7505P)

S Bacon 4/20/17

INTRODUCTION:

The registrant, Sergeant's Pet Care Products, Incorporated, is submitting an application to register the proposed end-use product, Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze on for Dogs. The active ingredients in this product are Imidacloprid, permethrin and Pyriproxyfen at label nominal concentrations of 8.80,44.0 and 0.44% a.i., respectively. This product is intended for use as an insecticide end-use product. In support of this request, the registrant is submitting a proposed basic Confidential Statement of Formula (CSF) dated 31 Aug 2016; a draft label and product chemistry data contained in MRID#s 500127-01 thru 500127-04. The Chemistry, Inerts and Toxicology Assessment Branch (CITAB) has been asked to review this submission.

SUMMARY OF FINDINGS:

1. Name of Active Ingredients: Imidacloprid (8.80% a.i.)
Permethrin (44.0% a.i.)
Pyriproxyfen (0.44% a.i.)

2. Has the registrant claimed substantial similarity to a registered product?

[ ] Yes; [X] No; [ ] NA; if yes give the registration number of the cited product.

3. All of the source materials of the active ingredient are derived from registered sources- [X] Yes [ ] No

4. All inert ingredients have been screened by IIAB and are approved for the proposed labeled uses.

5. Confidential Statement of Formula:

[X] Basic - Dated: 31 Aug 2016 Resubmitted Dated:
[ ] Alternate – Dated: Resubmitted Dated:

Alternate CSF complies with 40 CFR 152.43
[ ] Yes [ ] No [X] NA

6. Product label

a. Ingredient statement: Nominal concentration of AI listed on CSF concurs with product label (PR Notice 91-2).
[X] Yes, if not, explain below:

Is the sub statement in compliance with PR Notice 97-6 (inert ingredient vs other ingredient)
[X] Yes; [ ] No; if not, explain below

Metallic equivalent:	[ ] Yes	[X] NA
Soluble arsenic:	[ ] Yes	[X] NA
Isomeric ratios:	[ ] Yes	[X] NA
Acid Equivalent:	[ ] Yes	[X] NA

b. Health related sub statements: Product contains?

Petroleum distillate at > 10%:	[ ] Yes; [ ] No; [X] NA
Methanol at > 4%:	[ ] Yes; [ ] No; [X] NA
Sodium nitrate/sodium nitrite	[ ] Yes; [ ] No; [X] NA

c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for flammability, explosive potential or electric insulator breakdown?
[ ] Yes [X] No

Is the sub statement in compliance with PR Notice 98-6 (Total Release Fogger)?
[ ] Yes; [ ] No; [X] NA; if not, explain below

d. Label requires an additional Storage and Disposal statement: [ ] Yes [X] No; if yes explain below

7. Group **A**: Product Chemistry Data

CITAB's determination of the acceptability for the proposed product is listed in the tables below.

Guideline No.	**Study Title**		**Data submitted**		**CITAB's Assessment of Data**	**MRID Nos.**
			Yes	**No**		
830.1550	Product Identity & Composition		X		A	500127-01
830.1600	Description of materials used to produce the product		X		A	500127-01
830.1650	Description of formulation process		X		A	500127-01
830.1670	Discussion on the formation of impurities		X		A	500127-01
830.1700	Preliminary analysis			X	N/A	
830.1750	Certified limits (158.350)	Standard certified limits	X		A	see basic csf 8/31/16
		Proposed Limits				
		Justification for wider limits				
830.1800	Enforcement analytical method		X		A	500127-02

A = Acceptable, N = Not Acceptable, G = Data Gap, W = Waiver Request, I = In Progress, NA = Not Applicable; U = Upgradeable.

8. Group **B:**

Guideline No.	Study Title	Value or Qualitative Description	CITAB's Assessment of Data	MRID Nos.
830.6303	Physical State	Product is a yellowish, transparent liquid with a characteristic organic solvent odor.	A	500127-03
830.6314	Oxidation/ Reduction	Product does not contain oxidizing or reducing agents.	N/A	
830.6315	Flammability	Flashpoint: 102.8°C (217.0°F)	A	500127-03
830.6316	Explodability	Product does not contain explosive components.	N/A	
830.6317	Storage stability	Study to be conducted.	G	
830.6320	Corrosion Characteristics	Study to be conducted.	G	
830.7000	pH	4.43 (1% aq. solution)	A	500127-03
830.7100	Viscosity	12.6 cPs at 20°C (spindle# 1 30 rpm)	A	500127-03
830.7300	Density (units)	1.126 g/ml	A	500127-03

A = Acceptable, N = Not Acceptable, G = Data Gap, W = Waiver request, NA = Not applicable, I = In progress; U = Upgradeable.

CONCLUSIONS:

CITAB has reviewed the product chemistry data submitted for the proposed end-use product and has concluded that all conclusions are pending upon approval of all inert ingredients used in the formulation of this product.

A. Substantial similarity to the cited product (Reg. No. .....) from Product chemistry view point
[ ] Similar
[ ] Not similar, give reasons
[ ] Identical
[ ] Not identical
[X] Not applicable

B. Confidential Statement of formula

1. Basic CSF (dated 31 Aug 2016)
[X] Acceptable
[ ] Not Acceptable
[ ] Not Applicable

If not acceptable provide the reasons

2. Alternate CSF
[ ] Acceptable
[ ] Not Acceptable
[X] Not Applicable

If not acceptable give reasons

C. Group A Product Chemistry Data
[X] Acceptable
[ ] Not acceptable
[ ] Acceptable with the exception of Guideline(s): (provide the guideline number & explain)
[ ] Not required
[ ] Data cited

If the composition of the proposed product changes, then the product chemistry data requirements for product identity and composition (830.1550), description of the materials used to produce the product (830.1600) and description of the formulation process (830.1650 will require revision.

D. Group B Product chemistry data
[ ] Acceptable
[ ] Not acceptable
[X] Acceptable with the exception of Guidelines: (830.6317 & 830.63220)
[ ] Not required
[ ] Data cited

The registrant states that studies will be conducted for storage stability and corrosion characteristics.

E. Product Label/Draft Label
Recommendations – Yes [ ]; No [X]
If yes, give recommendations below:

Note: Please add additional remarks if necessary for each section

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

February 28, 2017

MEMORANDUM:

Subject:	Name of Pesticide Product:	SERGEANT'S IMIDACLOPRID + PERMETHRIN + PYRIPROXYFEN SQUEEZE ON FOR DOGS
	EPA Reg. No. /File Symbol:	2517-RTI
	DP Barcode:	DP 436235
	Decision No.:	521126
	Action Code:	R315
	Submission:	#991754
	E-Sub.	-
	PC Codes:	129099 (Imidacloprid: 8.8%) 109701 (Permethrin: 44%) 129032 (Pyriproxyfen: 0.44%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
Feb. 28, 2017

Through: John Redden, M.S., Senior Risk Assessor
CITAB
Registration Division (7505P)

JCR

To: Autumn Metzger / Laura Bacon RM04
IVB1
Registration Division (7505P)

Registrant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129099 Imidacloprid	8.80%
109701 Permethrin*	44.00%
129032 Pyriproxyfen	0.44%
Other Ingredients:	46.76%
TOTAL	100.00%

*cis/trans ratio: Max 55% (±) cis and min 45% (±) trans

ACTION REQUESTED: "Please review the MRIDs that are being cited for this new spot-on product and make sure 1) the products are substantially similar to each other and 2) the studies support this registration. You may also need to help CRP determine if CRP is required."

BACKGROUND: The registrant is citing MRIDs 470143-03 through 470143-08, which were originally submitted to support the formulations now registered under 11556-141, 11556-142, 11556-143 or 11556-144. However, the registrant has not claimed similarity to any registration on form 8570-1.

CITAB has previously addressed (review dated October 17, 2016) the companion animal safety studies cited to support the registration of 2517-RTI.

COMMENTS AND RECOMMENDATIONS:

1. The cited acute toxicity studies (MRIDs 470143-03 through -08) have been previously reviewed and classified as acceptable (TRB memorandum for 11556-RUR, dated June 6, 2007).

2. After comparing the CSF (dated August 31, 2016) for 2517-RTI and the composition of the test material used in the cited acute toxicity studies (see, for example, p. 3 of MRID 47014308_CA_2.pdf in Documentum), CITAB concludes they are toxicologically similar and the citations to MRIDs 470143-03 through -08 satisfy the acute toxicity data requirements for the registration of 2517-RTI.

3. Based on the results of the studies in MRIDs 470143-03 through -08, the following is the acute toxicity profile for 2517-RTI:

Oral LD_{50}	III	Cited	MRID 47014308
Dermal LD_{50}	IV	Cited	MRID 47014306
Inhalation LC_{50}	IV	Cited	MRID 47014305
Eye Irritation	II	Cited	MRID 47014307
Skin Irritation	III	Cited	MRID 47014304
Dermal Sensitization	Negative	Cited	MRID 47014303

4. Based on the acute toxicity profile given above and information from the CSF, the following are the precautionary and first aid statements for 2517-RTI, as obtained from the Label Review System:

PRODUCT ID #: **002517-00178**

PRODUCT NAME: **SERGEANT'S IMIDACLOPRID + PERMETHRIN + PYRIPROXYFEN SQUEEZE-ON FOR DOGS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

Hazards to Humans and Domestic Animals:

Causes substantial but temporary eye injury. Harmful if swallowed. Avoid contact with skin. Do not get in eyes or on clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

5. The registrant's proposed precautionary and first aid labeling statements (p. 8 of the Master Label dated 08 September 2016) are acceptable.

6. Based on the acute toxicity criteria in 40 CFR §157.22, 2517-RTI does not require Child-Resistant Packaging (CRP). It is also noted that EPA Reg. No. 11556-141 is not in CRP.

7. All acute toxicity data requirements for the registration of 2517-RTI have been satisfied by the citations to MRIDs 470143-03 through -08.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

DP BARCODE No.: D436234 **FILE SYMBOL No.**: 2517-RTI (screen) **DECISION No.**: 521126
PC Code: 109701,129032,129099 **Company Name:** Sergeant's Pet Care Products, Inc.
FOOD Use: No **ACTION CODE**: R 315 **PRODUCT NAME**: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs

DATE OUT: January 18, 2017

SUBJECT: Completeness Check Screen for End-Use Product

Product Name: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs

FROM: Bruce Kitchens, Chemist
Product Chemistry Team
Chemistry, Inerts and Toxicology Assessment Branch/RD (7505P)

Bruce Kitchens 1/18/17

TO: RM #04, Laura Bacon/Autumn Metzger
Invertebrate and Vertebrate Branch 1
Registration Division (7505P)

Company Name: Sergeant's Pet Care Products, Incorporated

Active Ingredients: Permethrin (44.0% a.i.)
Pyriproxyfen (0.44% a.i.)
Imidacloprid (8.80% a.i.)

MRID Nos.: 500127-01 thru 500127-04

CONCLUSION:

Deficiencies: No
(If there are deficiencies they are indicated below each heading as Note 1, Note 2 Etc).

Group A: All required data submitted

Group B: All data required submitted.

CSF: Basic CSF dated 31 Aug 2016

Product label: Yes

Note 1: The proposed basic CSF dated 31 Aug 2016 does not have the inert ingredient approval codes assigned to it. The inert ingredient codes must be assigned to the proposed basic CSF and returned to the product chemistry reviewer in order to complete the product chemistry evaluation.

Note to PM: If the deficiencies are found in the screen results, please inform the registrant and return to me the corrected deficiencies in response to 10-day letter, so that it can be attached to the original bean, if the data package is still in CITAB. New Bean is required in case the bean has been closed by CITAB. Thank you.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

October 17, 2016

Subject: SERGEANT'S IMIDACLOPRID+PERMETHRIN+PYRIPROXYFEN SQUEEZE-ON FOR DOGS
EPA File Symbol: 2517-RTI
DP Barcode 436236
Action Code: R315
PC Codes: 109701 (Permethrin: 35.6%)
129099 (Imidacloprid: 7.12%)
129032 (Pyriproxyfen: 0.36%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
Oct-17-2016

Through: Masih Hashim, Ph.D., Team Leader, Toxicology
CITAB
Registration Division (7505P)

Masih Hashim

To: Autumn Metzger/Laura Bacon RM 04
IVB1
Registration Division (7505P)

Applicant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
129099 Imidacloprid	8.80%
109701 Permethrin	44.00%
129032 Pyriproxyfen	0.44%
Other Ingredients:	46.76%
TOTAL:	100.00%

ACTION REQUESTED: "Please see the cited MRIDs the company is using to support this new spot on. Please determine if these MRIDs will support its registration…"

BACKGROUND: The proposed label and data matrix (dated 9/8/2016) for 2517-RTI are available in Documentum. The minimum age is 7 weeks. The proposed label indicates the formulation will be packaged in single dose applicators of 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs and puppies; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs and puppies; 0.085 fl. oz. (2.5 mL) for 21-55 lb dogs and puppies; and 0.135 fl. oz (4.0 mL) for dogs >55 lbs. The registrant is citing the following MRIDs to satisfy the 870.7200 data requirements: 47014309; 47014310; 45563003; 45097101; 44099801; 43679607; 43679608; 45097102; 45563002; 42182701 and 42178309.

COMMENTS AND RECOMMENDATIONS:

1. The study in MRID 47014309 was reviewed by TRB (June 6, 2007 memorandum for 11556-RUR). The following is from the executive summary:

   In a companion animal safety study (MRID 47014309), two groups, each containing 6 male and 6 female adult (11 ½ to 12 ½ months old) beagle dogs (Day -1 weights: males: 6.446 - 9.914 kg; females: 6.495 – 9.138 kg) were treated at a 5x fill volume/application (for dogs weighing 11-20 lbs the dose volume is 1.0 mL, or the amount that can be squeezed from an application tube; the fill volume for that tube is 1.05 mL, so each dog received 5 x 1.05 mL or 5.25 mL; likewise, dogs weighing 20-55 lbs were treated with 5x the fill volume of 2.58 mL or 12.9 mL). Dogs in the control group received an application of mineral oil, while dogs in the 5x test material group were dosed with the Imidacloprid-Permethrin-Pyriproxifen formulation as proposed for registration. Dogs were treated on Days 0, 7, 14 and 21 (label instructions specify once-a-month dosing, so the cumulative dose of the 5x group over a 21-day period was 20x the normal use exposure).

   All dogs survived and there was no indication of any effects on body weight or food consumption. No neurological effects, abnormalities or any other indications of toxicity were observed. Sporadically statistically significant differences in hematology and/or clinical chemistry parameters were not biologically relevant, and values were generally within the historical control ranges of the performing laboratory. Overall, there were no indications of any effects on hematology or clinical chemistry parameters.

   *This study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) for adult dogs, and demonstrates a greater than 5X margin of safety for the proposed use of this formulation on adult dogs.*

2. The study in MRID 47014310 was reviewed (June 6, 2007 memorandum for 11556-RUR) by TRB and was classified as Invalid. This study cannot be used to support the proposed use of 2517-RTI on 7-week (and older) puppies.

3. The study in MRID 45563003 supported the following Advantix registrations: 11556-132, -133, -134 and -135; all with declarations of 8.8% imidacloprid and 44.0% permethrin (no pyriproxyfen). The following is from the executive summary of a TRB review for 11556-132 dated June 28, 2002:

   In a companion animal safety study (MRID 45563003) Imidacloprid (8.84% w/w) and Permethrin (43.73% w/w) Topical Solution (Lot No. A-01-048-G804-01-02-11), containing 100.8 mg of imidacloprid and 498.5 mg permethrin per mL, was dermally applied as a single 2 mL (5X the proposed use dosage rate of 0.4 mL) dose to the dorsal cervical area of each puppy in a group of

6 male and 6 female young (≤ 7 weeks old at initiation of dosage) on days 0, 7, 14 and 21. (The proposed 1X rate is 0.4 mL for dogs and puppies weighing ≤ 10 lbs; 1.0 mL for dogs weighing 11-20 lbs; 2.5 mL for dogs weighing 21-55 lbs, and 4.0 mL for dogs weighing ≥ 55 lbs.) A second (control) group of 6 male and 6 female dogs of the same age received an application of 1.0 mL vehicle (formulation without active ingredients) on days 0, 7, 14 and 21. For test group males on day 0 individual doses ranged from 931.4 mg test substance (82.3 mg Imidacloprid and 407.3 mg Permethrin)/kg to 1614 mg test substance (142.7 mg Imidacloprid and 795.6 mg Permethrin)/kg. In test group females individual doses on day 0 ranged from 1220.6 mg test substance (107.9 mg Imidacloprid and 533.7 mg Permethrin)/kg to 1581.1 mg test substance.

It is noted that not only were these puppies treated at a 5X single-dose application rate, but that they were also given four 5X treatments in a 21-day period (as the label specifies once-a-month treatment at the 1X label, these puppies then received a cumulative of 20X the monthly dose specified on the label).

This study generally followed the pertinent guidelines for a companion animal safety study (OPPTS 870.7200).

The study is classified as Acceptable in demonstrating an adequate (approximately 5X in terms of overt symptoms) margin of safety. While treated puppies did not eat as much as their controls following on days 1 and 8 following applications of the test material on days 0 and 7, their food consumption recovered in a day or so, and there was little or no evidence of any reduction in food consumption following the third and fourth applications of the test material.

4. In a TRB memorandum for 11556-132 dated June 17, 2013, the following was stated:

   According to our records, the companion animal (7 week-old puppy) safety study data requirement for this product was satisfied by the study in MRID 45563003). The study in MRID 45563003 was conducted on an Imidacloprid (8.84%) + Permethrin (43.73%) formulation and has been classified as acceptable (TXR 5002455, TRB memorandum dated June 28, 2002).

   In the study in MRID 45563003 2.0 mL (5 x 0.4 mL) of test material was topically applied to each of 12 Group B puppies on Days 0, 7, 14 and 21. On Day 0 the mean weights ± S.D. of Group B puppies were the following (calculated from data on pages 38-39 of MRID 45563003): males: 2010 ± 360.7 (= 4.43 ± 0.80 lbs); females: 1645 ± 164.9 (=3.62 ± 0.36 lbs); combined: 1827.5 ± 328.4 g (= 4.03 ± 0.72 lbs). Taking the 4 male and 4 female least weight puppies would give a mean weight of 1697 ± 251 g (= 3.74 ± 0.55 lb).

   Based on the Day 0 mean body weights of the puppies in the study in MRID 45563003 TRB concludes that the appropriate statement is: "Do not apply to puppies weighing less than 4 lbs."

5. The study in MRID 45097101 was reviewed by TRB (September 8, 2000 memorandum for 11556-125). The following is from the executive summary:

In a companion animal safety study (MRID 45097101), Advantage Plus® for Dogs (Active Ingredients: 9.1% Imidacloprid w/w; 0.9% Pyriproxyfen w/w) was applied topically at a dose of 2.0 mL/puppy (5X the label specified dose of 0.4 mL/puppy for puppies ≤10 lbs) to a group of 7 male and 7 female beagle puppies, seven weeks of age at the time of first treatment. Individual weights of the puppies in the treatment group ranged from 2.54 to 4.01 lbs (1.15-1.82 kg) on day -1. Controls (7M, 7F; weight range: 2.49-5.03 lbs; 1.13-2.29 kg) were dosed with the vehicle alone at a dose of 2.0 mL/puppy (5.6X the volume of the vehicle present in the specified dose). Both groups were treated on study days 0, 7, 14, and 21. The recommended label dose is once a month. However, the labeling for these products includes the statement: "If re-treatment becomes necessary earlier than four weeks, do not re-treat more than once weekly."
There were no deaths during the study. Following all treatments, a rough hair coat condition at the application site was noted on 3-14 puppies of both groups, and white powder was occasionally noted at the application sites; however, there were no signs of irritation. One puppy from the test substance group was found to have ocular discharge and "crusty patches" on its ventral abdomen, by the lip and under each eye on study day 36. The puppies completed treatment for coccidiosis on study day -8. During the remainder of acclimation, in the test substance group there were two observations of loose feces with mucous and five observations of diarrhea, with or without mucous or red colored mucous, exhibited by four animals. In the vehicle control group, there were two observations of loose feces with mucous, exhibited by two animals.

Despite the fact that the puppies may not have been entirely free of infection, and despite some deficiencies in the reporting of the data, the study is classified as ***Acceptable*** *as a companion animal safety study (OPPTS 870.7200) in puppies. The lack of any indications of a consistent toxicological response following exposures (a total of 4) to 5X label-specified use applications of the test material indicates that an adequate safety margin exists for this formulation and its proposed use on puppies 7 weeks of age and older.*

6. In a September 10, 2007 TRB memorandum for 11556-RUR it was stated that the puppy study requirement (which would include the 4 lb minimum weight and 7 week minimum age) for EPA File Symbol 11556-RUR was satisfied by bridging from the two studies in MRIDs 45097101 and 45563003, taking into consideration the low toxicity of pyriproxyfen (as indicated in MRID 42178309) to mammalian species.

7. The study in MRID 44099801 was reviewed by HED (TXR 0012322, sign-off date 9/24/97). The following is from the executive summary:

In a domestic animal safety study (MRID # 44099801), six 7 week-old puppies/sex were treated with Advantage™ (9.1% imidacloprid) at 5X the recommended use rate (2.0 ml if < 10 lbs; 5.0 ml if > 10 lbs) at weekly intervals for eight treatments. Six puppies/sex were treated with the vehicle control at the recommended use rate (0.4 ml if < 10 lbs; 1.0 ml if > 10 lbs) at weekly intervals for eight treatments. There was no evidence of treatment-related toxicity in clinical signs or clinical pathology parameters. All animals gained weight during the study. It was demonstrated that 7 week-old puppies can tolerate a dose of 5X the recommended use rate.

The study is considered acceptable and satisfies the draft guideline requirements (81-6) for a domestic animal safety study.

8. The study in MRID 43679607 was reviewed in HED (TXR 0011821, 03/05/96) with the following summary:

Nine adult dogs of mixed breed (3 males, 6 females, one male and two females/group) were dermally exposed to Imidacloprid, 10% Spot-On. Dose levels were 50 mg/kg/day x 1 day, and 50/mg/kg/day x 3 days. Controls received placebo (formulation less active ingredient) at 50/mg/kg/day x 3 days. Animals then were observed for 14 days.

No major treatment related dermal, clinical signs, body weight effects or clinical chemistry changes were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that adult dogs can tolerate up 50 mg/kg without significant reactions.

This acute dermal study is classified as Acceptable when combined with another study, and satisfies the requirements for a domestic animal study in the dog, 18 lb (8 kg) body weight and above. The number of animals/group is too small and not in keeping with general study practice. However, when data are combined with the companion study in the dog (MRID 43679608), the information is considered useful.

9. The study in MRID 43679608 was reviewed in HED (TXR 0011821, 03/05/96) with the following summary:

18 adult dogs of various breeds (3 males and 3 females / group) were dermally exposed to Imidacloprid, 10% Spot-On formulation at seven-day intervals for a total of eight treatments. Dose levels were 10 or 50 mg/kg. Controls received placebo (formulation less active ingredient) at 50/mg/kg.

No major treatment related dermal, clinical signs, body weight effects or clinical chemistry/hematology were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that adult dogs can tolerate up to 50 mg/kg of the active ingredient without significant reactions. Inadequate testing was done in dogs less than four months old.

This repeated dose dermal study is classified as Acceptable and satisfies the requirements for a General Safety Evaluation for Topical Use (86-1) in the dog.

10. The study in MRID 45097102 was reviewed by TRB (September 8, 2000 memorandum for 11556-125). The following is from the executive summary:

In a companion animal safety study (MRID 45097102) with adult beagles (ages ranging from 1 year and 3 months to 6 years), Advantage Plus® for Dogs (Active Ingredients: 9.1% Imidacloprid w/w; 0.9% Pyriproxyfen w/w) was applied topically at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs.(five times the recommended dose) to groups of 6 male and 6 female dogs. Eight dogs were consistently dosed with 12.5 mL of the formulation/application, and four were consistently dosed with 5 mL/application. Controls were dosed with the vehicle at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs.(5.6 times the volume of the vehicle present in the recommended dose). Five dogs were consistently treated with 12.5 mL vehicle/application, five were consistently dosed with 5 mL/application, and two dogs received 12.5 mL/application for the first, second and fourth

applications, and 5.0 mL/application for the third application. Dogs were treated on study days 0, 7, 14, and 21.

There were no deaths during the study. The dogs received no concomitant medication or therapy during the treatment period. The most prominent clinical sign was a rough appearance of the hair coats on dogs from both groups following treatment and lasting for up to 36 hours; however, there were no signs of irritation at the application sites. Several dogs from both groups, "jumped excessively due to excitement" on study day 21. The study report did not indicate which dogs. Three dogs (two from the test substance group and one from the vehicle control group) also exhibited sore footpads on that date. These findings for day 21 were not noted at any other time during the study. There were no treatment related effects on body weights, food consumption, or clinical pathology parameters.

It is also noted that the proposed products (containing approximately 9% Imidacloprid, but only 0.46% pyriproxyfen, rather than the 0.9% in the formulation as tested) are similar to existing registered products containing 9% Imidacloprid as sole active. Pyriproxyfen is known to have a low toxicity to mammalian species.

The study is classified as ***Acceptable/Guideline*** *as a companion animal safety study.*

11. The study in MRID 45097102 was reviewed by TRB (memorandum dated September 8, 2000 for 11556-REL). The following is from the executive summary:

In a companion animal safety study (MRID 45097102) with adult beagles (ages ranging from 1 year and 3 months to 6 years), Advantage Plus® for Dogs (Active Ingredients: 9.1% Imidacloprid w/w; 0.9% Pyriproxyfen w/w) was applied topically at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs.(five times the recommended dose) to groups of 6 male and 6 female dogs. Eight dogs were consistently dosed with 12.5 mL of the formulation/application, and four were consistently dosed with 5 mL/application. Controls were dosed with the vehicle at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs.(5.6 times the volume of the vehicle present in the recommended dose). Five dogs were consistently treated with 12.5 mL vehicle/application, five were consistently dosed with 5 mL/application, and two dogs received 12.5 mL/application for the first, second and fourth applications, and 5.0 mL/application for the third application. Dogs were treated on study days 0, 7, 14, and 21.

There were no deaths during the study. The dogs received no concomitant medication or therapy during the treatment period. The most prominent clinical sign was a rough appearance of the hair coats on dogs from both groups following treatment and lasting for up to 36 hours; however, there were no signs of irritation at the application sites. There were no treatment related effects on body weights, food consumption, or clinical pathology parameters.

The study is classified as ***Acceptable/Guideline*** *as a companion animal safety study (OPPTS 870.7200) in dogs. The lack of any consistent indications of a toxicological response following exposures (a total of 4) to 5X label-specified use applications of the test material indicates that an adequate safety margin exists for this formulation and its proposed use on adult dogs.*

11. The study in MRID 45563002 was reviewed by TRB (June 28, 2002 memorandum for 11556-RGE). The following is from the executive summary:

In a companion animal safety study (MRID 45563002) Imidacloprid (8.8% w/w) and Permethrin (44.0% w/w) Topical Solution (Lot No. A-01-061-G804-01-02-78), containing 99.6 mg of imidacloprid and 496.8 mg permethrin per mL, was administered via syringe to the dorsal midline of each dog in a group of 6 male and 6 female young adult (10-11 months old) beagles at 5X the proposed use dosage rate on days 0, 7, 14 and 21. (The proposed 1X rate is 0.4 mL for dogs weighing ≤ 10 lbs; 1.0 mL for dogs weighing 11-20 lbs; 2.5 mL for dogs weighing 21-55 lbs, and 4.0 mL for dogs weighing ≥ 55 lbs.) A second (control) group of 6 male and 6 female dogs of the same age received a weekly 5X application of the test substance less the active ingredients on days 0, 7, 14 and 21. All test material males and 4/6 females received 12.5 mL/week/dog; 2/6 females consistently received 5.0 mL/week/dog. All placebo group males and 3/6 females received 12.5 mL/week/dog; 3/6 females consistently received 5.0 mL/week/dog. For test group males exposure to the actives ranged from 85.9 to 132.4 mg Imidacloprid/kg body weight and from 428.3 to 660.7 mg permethrin/kg body weight. For females, ranges were from 55.6 to 122 mg Imidacloprid/kg and from 279.2 to 608.9 permethrin/kg.

No mortality occurred. The report states that there was no evidence of adverse or irreversible clinical signs demonstrated by the animals on the days of dosing or at other times during the study. However, there were noticeable reductions in mean food consumption for both the placebo and 5X groups on days -12, -5, 1, 22, 39, and, to a lesser extent, for days 8 and 15 (the vehicle or test material was administered on days 0, 7, 14 and 21). The reduced food consumptions on days -12, -5, 1, 22 and 39 were presumably largely due to blood taking and/or overnight fasting, which (for days 1 and 22) would have masked any effects from exposure to the test material. However the reductions for days 8 and 15 (Day 8 relative to day 7: vehicle males: -24.9%; 5X males: -11.4%; vehicle females: -14.9%; 5X females: -15.0%; Day 15 relative to day 14: vehicle males: -41.2%; 5X males: -46.0%; vehicle females: -15.0%; 5X females: -31.9%) were presumably associated with administration of the vehicle and test material (the vehicle is not toxicologically inert). Mean food consumption values recovered in all groups for days 9 and 15.

There were sporadic occurrences of vomiting, mucoid feces, with a "clustering" of these around day 1. These may have resulted from stress on the dogs from the combination of fasting, blood taking and exposure to the vehicle or test material.

A number of dogs in both the vehicle and 5X groups showed a "few" to "multiple" pinpoint-sized red areas at the base of hair shafts at the dose site on days 7, 14 and/or 21. In one case, these red areas persisted for several days.

All animals survived to the end of the study, and there were no terminal sacrifices (not required for this type of study).

It is noted that not only were these test material treated dogs received a 5X single-dose application rate, but that they were also given four 5X treatments in a 21-day period (as the label specifies once-a-month treatment at the 1X label, these dogs then received a cumulative of 20X the monthly dose specified on the label).

This study generally followed the pertinent guidelines for a companion animal safety study (OPPTS 870.7200), and is classified as Acceptable in demonstrating an adequate (approximately 5X in terms of overt symptoms) margin of safety. While administration of the vehicle or test material on days 7 and 14 was followed by a decrease in food consumption on days 8 and 15, food consumption quickly recovered in a day or so.

12. The studies in MRIDs 42182701 (Driver, J.; Oonnithan, S.; Paynter, O.; et al. (1991) Evaluation of the Toxicology and Potential Health Risks Associated with Indoor, Nonfood Uses of Sumilarv. Unpublished study prepared by Technology Services Group, Inc. 71 p) and 42178309 (Chapman, E. (1991) S31183: Toxicity Study by Oral (Capsule) Administration to Beagle Dogs for 52 Weeks (Sumilarv Technical Grade): Lab Project Number: 91/0776. Unpublished study prepared by Life Science Research Ltd. 320 p.) adequately demonstrate that pyriproxyfen has a low toxicity to mammalian species.

13. All Companion Animal Safety (870.7200) requirements for the registration of 2517-RTI have been satisfied by the citations provided in the data matrix dated 9/8/2016. These citations also support the label-specified minimum weight (4 lbs) and age (7 weeks) for dogs/puppies, as well as the proposed dosage levels and weight ranges (0.014 fl. oz. (0.4 mL) for 4-10 lb dogs and puppies; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs and puppies; 0.085 fl. oz. (2.5 mL) for 21-55 lb dogs and puppies; and 0.135 fl. oz (4.0 mL) for dogs >55 lbs).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

September 13, 2016

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

EXPONENT, INC.
SERGEANT'S PET CARE PRODUCTS, INC.
1150 CONNECTICUT AVE. NW, SUITE 1100
WASHINGTON, DC 20036

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 08-SEP-16. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

PRIA 3 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

September 2012

21 Day Screen Start Date: 9-8-16

Experts In-Processing Signature: B.B. Date 9-12-16 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 2517-RTI	EPA Receipt Date: 9-8-16

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4)			X		
	a) All inerts, including fragrances, approved for the proposed uses (see Footnote A)	yes	no			
			X			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes	no			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) completed and signed (N/A if source is unregistered or applicant owns the technical)			X		
5	**Data Matrix** (EPA Form 8570-35) both internal and external copies (PR 98-5) completed and signed (N/A if 100% repack)			X		
		yes	no			
	a) Selective Method (Fee category experts use)	X				
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label (Electronic labels on CD are encouraged and guidance is available)**			X		
7	**Is the data package consistent with PR Notice 86-5**			X		
8	**Notice of Filing included with petitions**					X

9	**If applicable for conventional applications, <u>reduced risk rationale</u>**			X
10	**<u>Required Data</u> and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

Documentation: Pass or Fail
-All Required Forms Complete

Inerts: Pass or Fail
- Inert not found
- Submitter contacted 9/14/16
- Inert Petition has been submitted simultaneously
- Failed until further examination by PM

PRN 11-03: Pass or Fail
- MRID: 500127

9/15/16

Overall Status: Pass or Fail

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses or have an application pending with the Agency. If an unapproved inert with no application pending with the Agency is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses or have an application pending with the Agency **even if a product is currently registered** by consulting the inert Web site and if the inert is not approved nor has an application pending with the Agency, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch.

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Provide the required information necessary to identify an inert approval application that is pending with the Agency; or

3. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

4. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R300 or R301), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

KELLY HOSKINS
SERGEANT'S PET CARE PRODUCTS, INC.
10077 SOUTH 134TH STREET
OMAHA, NE 68138-3710

RE: Application for Registration dated: 08-SEP-16
Date Fee Payment: 08-SEP-16
Product Name: SERGEANT'S IMIDACLOPRID + PERMETHRIN + PYRIPROXYFEN SQUEEZE ON FOR DOGS
EPA Registration Number: 2517-RTI
Decision Number: D-521126

Dear Registrant:

The Agency has completed its initial contents screen of your application pursuant to Section 33(f)(4)(B) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended the Pesticide Registration Improvement Renewal Act. The Agency has determined that your application did not pass the initial contents screen and therefore must be rejected.

Specifically, the jacket was rejected because an inert included in the formulation is still in the process of being approved.

Furthermore, pursuant to FIFRA Section 33(b)(2)(G) the Agency must retain 25% of the registration service fee. Any future submissions to the Agency will be considered a new application and subject to the full registration service fee and another initial contents screen of all necessary fees, forms, data, and draft labeling.

Sincerely,

XXXXXXXX, Director
Office of Pesticide Programs

Varner, Stephanie

From: Kelly Hoskins <Kelly.Hoskins@perrigo.com>
Sent: Thursday, September 15, 2016 9:09 AM
To: Varner, Stephanie
Subject: RE: Submission to EPA: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs (EPA Reg. No. 2517-RTI)

No problem.

Kelly Hoskins | Manager of Regulatory Affairs
Sergeant's Pet Care Products, Inc. dba Perrigo Animal Health
10077 South 134th Street
Omaha, NE 68138-3710
T: (402) 938-7079
E: kelly.hoskins@perrigo.com | perrigoanimalhealth.com

Quality Affordable Healthcare Products® for Pets!

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Animal Health

From: Varner, Stephanie [mailto:Varner.Stephanie@epa.gov]
Sent: Thursday, September 15, 2016 8:08 AM
To: Kelly Hoskins
Subject: RE: Submission to EPA: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs (EPA Reg. No. 2517-RTI)

Hi Kelly,
I was about to email you back actually. I just got the application for the Inert so it's all cleared up. Sorry for the mix up!
Thanks,
Stephanie

From: Kelly Hoskins [mailto:Kelly.Hoskins@perrigo.com]
Sent: Thursday, September 15, 2016 9:06 AM
To: Varner, Stephanie <Varner.Stephanie@epa.gov>
Cc: Prince Bamaze <Prince.Bamaze@perrigo.com>; 'James Messina' <jmessina@exponent.com>; Reginald Coler <rcoler@exponent.com>; 'Mary Hunt' <mhunt@exponent.com>
Subject: RE: Submission to EPA: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs (EPA Reg. No. 2517-RTI)

Stephanie,
Thank you for contacting us, yes we are aware [redacted] is not on the Inerts list, at the time of this submission we also filed an Inert Petition at the same time with the required information and I have attached the cover letter for that submission.

If you have any additional questions please let me know.

Kelly Hoskins | Manager of Regulatory Affairs
Sergeant's Pet Care Products, Inc. dba Perrigo Animal Health
10077 South 134th Street
Omaha, NE 68138-3710
T: (402) 938-7079
E: kelly.hoskins@perrigo.com | perrigoanimalhealth.com

Quality Affordable Healthcare Products® for Pets!

Perrigo
Animal Health

From: Varner, Stephanie [mailto:Varner.Stephanie@epa.gov]
Sent: Wednesday, September 14, 2016 10:36 AM
To: Kelly Hoskins
Subject: Submission to EPA: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs (EPA Reg. No. 2517-RTI)

Dear Ms. Hoskins,

My name is Stephanie Varner, and I am a contractor with the EPA. I am contacting you in regards to your submissions in support of the product Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs (EPA Reg. No. 2517-RTI). We have found a deficiency with the submissions that will need to be addressed:

1. There was an issue with the submitted CSF. Please see the attached Inert Clearance Form for further explanation.

Thank you!

Stephanie Varner

Contractor, US EPA
2777 S. Crystral Drive, S-4813
Arlington, VA 22202
(703) 347-0240
Email: varner.stephanie@epa.gov

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

September 9, 2016

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP Decision Number: D-521126
EPA File Symbol or Registration Number: 2517-RTI
Product Name: Sergeant¿s Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs
EPA Receipt Date: 08-Sep-2016
EPA Company Number: 2517
Company Name: SERGEANT'S PET CARE PRODUCTS, INC.

KELLY R. HOSKINS
SERGEANT'S PET CARE PRODUCTS, INC.
PO Box 540399
OMAHA, NE 68154-0399

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R315

NEW END-USE NON-FOOD ANIMAL PRODUCT WITH SUBMISSION OF TWO OR MORE TARGET ANIMAL SAFETY STUDIES;INCLUDES DATA AND/OR WAIVERS OF DATA FOR ONLY:;PRODUCT CHEMISTRY;ACUTE TOXICITY;PUBLIC HEALTH PEST EFFICACY);ANIMAL SAFETY STUDIES;CHILD RESISTANT PACKAGING;

No additional payment is due at this time. If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-9362.

Sincerely,

Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{991754?~

This package includes the following

- (•) New Registration
- ( ) Amendment

[x] Studies? [ ] Fee Waiver?

[ ] volpay % Reduction: ___

for Division

- ( ) AD
- ( ) BPPD
- (•) RD

Risk Mgr. 4

Receipt No. S-	991754
EPA File Symbol/Reg. No.	2517-RTI
Pin-Punch Date:	9/8/2016

[ ] This item is NOT subject to FFS action.

Action Code:

Requested: R315

Granted: R315

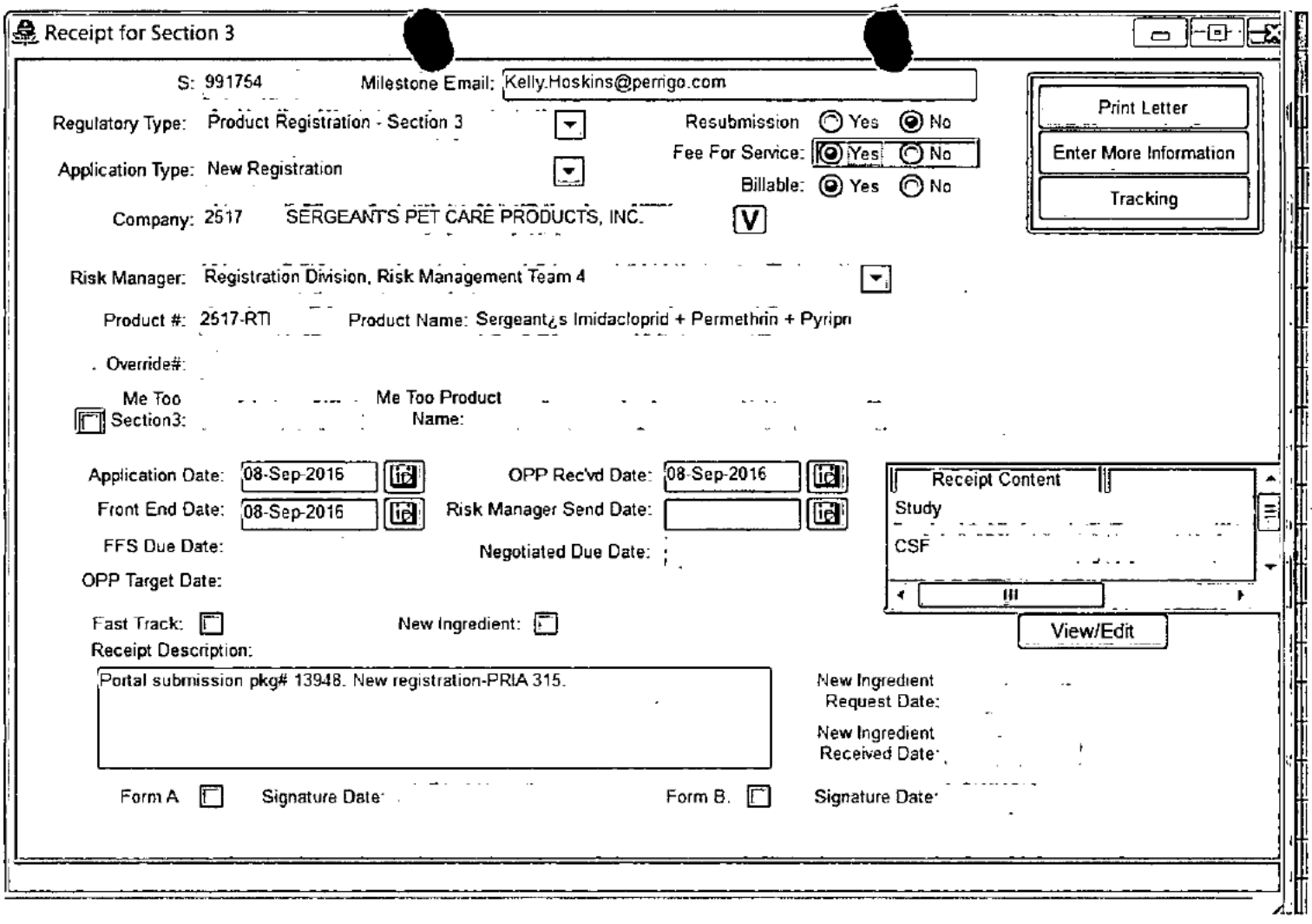
Amount Due: $ 8,820.00

Parent/Child Decisions:

[ ] Inert Cleared for ~~Intended~~ Use [ ] Uncleared Inert in Product

Reviewer: _____ Date: 9-9-16

Remarks: -similarity clinic


Receipt for Section 3
S: 991754
Milestone Email: Kelly.Hoskins@perrigo.com
Regulatory Type: Product Registration - Section 3
Application Type: New Registration
Company: 2517 SERGEANT'S PET CARE PRODUCTS, INC.
Resubmission Yes No
Fee For Service: Yes No
Billable: Yes No
Print Letter
Enter More Information
Tracking
Risk Manager: Registration Division, Risk Management Team 4
Product #: 2517-RTI
Product Name: Sergeant¿s Imidacloprid + Permethrin + Pyripn
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 08-Sep-2016
Front End Date: 08-Sep-2016
FFS Due Date:
OPP Target Date:
OPP Rec'vd Date: 08-Sep-2016
Risk Manager Send Date:
Negotiated Due Date:
Receipt Content
Study
CSF
View/Edit
Fast Track:
New Ingredient:
Receipt Description:
Portal submission pkg# 13948. New registration-PRIA 315.
New Ingredient Request Date:
New Ingredient Received Date:
Form A
Signature Date:
Form B.
Signature Date:

DOCUMENTUM

From: Mary Hunt
To: Reginald Coler
Subject: FW: Pay.gov Payment Confirmation: PRIA Service Fees
Date: Wednesday, September 07, 2016 7:21:51 PM

-----Original Message-----
From: Prince Bamaze [mailto:Prince.Bamaze@perrigo.com]
Sent: Wednesday, August 31, 2016 3:10 PM
To: Mary Hunt
Cc: Kelly Hoskins; Mark Levin; Prince Bamaze; James Messina
Subject:-FW: Pay.gov Payment Confirmation: PRIA Service Fees

Prince Bamaze | Regulatory Affairs Associate Perrigo Animal Health
T: (402) 938-7065
F: (402) 938-7165
E: prince.bamaze@perrigo.com | perrigoanimalhealth.com

-----Original Message-----
From: notification@pay.gov [mailto:notification@pay.gov]
Sent: Wednesday, August 31, 2016 2:02 PM
To: Prince Bamaze
Subject: Pay.gov Payment Confirmation: PRIA Service Fees

Your payment has been submitted to Pay.gov and the details are below. To confirm that the payment processed as expected, you may refer to your bank statement on the scheduled payment date. If you have any questions or wish to cancel this payment, you will need to contact the agency you paid at your earliest convenience.

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 25TKOV9U
Agency Tracking ID: 75083097831

Account Holder Name: Sergeants Pet Care Products Inc
Transaction Type: ACH Debit
Transaction Amount: $8,820.00
Payment Date: 09/01/2016
Account Type: Business Checking
Routing Number: 121100782
Account Number: **********0100

Transaction Date: 08/31/2016 03:01:30 PM EDT
Total Payments Scheduled: 1
Frequency: OneTime

Registration Number: 2517-NEW
Company Name: Sergeant's
Company Number: 2517
Action Code: R315

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:

Sergeant's Pet Care Products, Inc.
10077 South 134th Street
Omaha, NE 68138-3710

CONTACT PERSON (Return to)

James Messina
Exponent, Inc.
1150 Connecticut Ave. NW, Suite 1100
Washington, DC 20036

REGULATORY ACTION SUPPORTED BY THIS PACKAGE:

This submission is prepared to support an EPA registration application for the new end-use product, Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs.

SUBMITTAL DATE:

September 8, 2016

Volume	Study Title	MRID No.
1	Administrative Materials	50012700
2	Product Identity and Composition, Description of the Materials Used, Description of the Formulation Process, Discussion of the Formation	50012701
3	Enforcement Analytical Methods Validation for Sergeant's Permethrin + Imidacloprid + Pyriproxyfen Squeeze On for Dogs	50012702
4	Application for Registration of Sergeant's Imidacloprid – Pyriproxyfen – Permethrin Squeeze-on for Dogs Physical and Chemical Characteristics	50012703
5	Summary of Group B Product Chemistry Waivers for Sergeant's Permethrin + Imidacloprid + Pyriproxyfen Squeeze On for Dogs	50012704

Pages 103-104 Claimed confidential by submitter

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☒ Registration ☐ Amendment ☐ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: Sergeant's Pet Care Products Inc. / 2517-NEW
2. EPA Product Manager: Laura Bacon
3. Proposed Classification: ☒ None ☐ Restricted
4. Company/Product (Name): Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs
5. PM 4
5. Name and Address of Applicant *(Include ZIP Code)*: Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 6813
☐ *Check if this is a new address*
6. **Expedited Review**. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:
EPA Reg. No. ABM-based on 11556 - 141, 142, 143, 144
Product Name

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

PRIA Category R315. Please see cover letter for further details.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging: ☐ Yes* ☒ No
Certification must be submitted

Unit Packaging: ☒ Yes ☐ No
If "Yes" Unit Packaging wgt. 0.014 fl oz, 0.034 fl oz, 0.085 fl oz, 0.135 fl oz
No. per Container: 1 up to 24

Water Soluble Packaging: ☐ Yes ☒ No
If "Yes" Package wgt.
No. per Container

2. Type of Container: ☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag

3. Location of Net Contents Information: ☒ Label ☐ Container

4. Size(s) Retail Container: 0.014 fl oz, 0.034 fl oz, 0.085 fl oz, or 0.135 fl oz tubes (1 up to 24 tubes)

5. Location of Label Directions: ☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product: ☐ Lithograph ☒ Other printed ☐ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Kelly R. Hoskins	Manager of Regulatory Affairs	402-938-7079

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature BY: Kelly R Hoskins
3. Title: Manager of Regulatory Affairs
4. Typed Name: Kelly R. Hoskins
5. Date: September 8, 2016

DOCUMENTUM

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M STREET, S.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	2517-NEW
Active Ingredient(s) and/or representative test compound(s) Permethrin, Imidacloprid, Pyriproxyfen	Date September 8, 2016
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor, Nonfood.	Product Name Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulators Exemption Statement (EPA Form 8570-27)

☐ *I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form* should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose)	☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method, or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section 1, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitted to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment of both under applicable law.

Signature	Date	Typed or Printed Name and Title
Kelly R Hoskins	9/8/2016	Kelly R. Hoskins, Manager of Regulatory Affairs Sergeant's Pet Care Products, Inc

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

Form Approved. OMB No. 2070-0060. Approval expires 5-31-98

United States
Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152.85)

Applicant's Name and Address	**EPA File Symbol/Registration Number**
Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	2517-NEW
	Product Name *Sergeant's Imidacloprid + Permethrin +Pyriproxyfen Squeeze On for Dogs*
	Date of Confidential Statement of Formula ***(EPA Form 8570-4)*** August 31, 2016

As an authorized representative of the applicant for registration of the product identified above, I certify that:

(1) This product contains the following active ingredient(s):
Permethrin, Imidacloprid, Pyriproyfen

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging another product which contains that active ingredient which is registered under FIFRA Section 3, is purchased by us from another producer, and is labeled for at least each use for which my product is proposed to be labeled.

(3) Indicate by checking (A) or (B) below which paragraph applies:

[X] (A) An accurate Confidential Statement of Formula (*EPA FORM 8570-4*) for the above identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1)

OR

[ ] (B) The Confidential Statement of Formula (CSF) (EPA Form 8750-4) referenced above and on file with the EPA is complete, current, and accurate and contains the information required on the current CSF

(4) The following active ingredients in this product qualify for the formulator's exemption

Source		
Active Ingredient	**Product Name**	**Registration Number**
Imidacloprid (98.3%) Pyriproxyfen (98.7%) Pyriproxyfen (98.4%) Pyriproxyfen (98.7%) Pyriproxyfen (98.7%) Permethrin (95.5%) Permethrin (95.5%) Permethrin (95.5%)	[redacted]	

Product ingredient source information may be entitled to confidential treatment

Signature	**Name and Title**	**Date**
Kelly R Hoskins	Kelly R. Hoskins, Manager of Regulatory Affairs	September 8, 2016

EPA Form 8570-27 (Rev. 8-95)

White - EPA copy
Yellow - Applicant copy

*U.S. GPO: 1995-388-820/20413

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: September 8, 2016	EPA Reg No./File Symbol 2517-NEW	Page 1 of 4
Applicant's/Registrant's Name & Address Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	**Product:** Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs	

Ingredients: Imidacloprid, Permethrin, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Product Chemistry					
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1700, 830.1750	Product Identity and Composition, Description of the Materials Used, Description of the Formulation Process, Discussion of the Formation of Impurities and Certified Limits for Permethrin + Imidacloprid + Pyriproxyfen Squeeze On for Dogs	50012701	Sergeant's Pet Care Products, Inc.	OWN	
830.1800	Enforcement Analytical Method Validation for Permethrin + Imidacloprid + Pyriproxyfen Squeeze On for Dogs	50012702	Sergeant's Pet Care Products, Inc.	OWN	
830.6302, 830.6303, 830.6304, 830.1500, 830.7000, 830.7100, 830.7300	Application for Registration of Sergeant's Imidacloprid – Pyriproxyfen – Permethrin Squeeze-on for Dogs Physical and Chemical Characteristics	50012703	Sergeant's Pet Care Products, Inc.	OWN	
830.6313, 830.6314, 830.6316, 830.6319, 830.6321, 830.7520	Summary of Group B Product Chemistry Waivers for Sergeant's Permethrin + Imidacloprid + Pyriproxyfen Squeeze On for Dogs	50012704	Sergeant's Pet Care Products, Inc.	OWN	
830.6317, 830.6320	Storage Stability and Corrosion Characteristics	To be conducted	Sergeant's Pet Care Products, Inc.		
Acute Toxicity					
870.1100	Durando, J. (2005) Imidacloprid/Permethrin/Pyriproxyfen: Acute Oral Toxicity Up and Down Procedure in Rats	47014308	Bayer Healthcare LLC	PAY	
870.1200	Moore, G. (2006) Imidacloprid/Permethrin/Pyriproxyfen: Acute Dermal Toxicity Study in Rats - Limit Test	47014306	Bayer Healthcare LLC	PAY	
870.1300	Durando, J. (2006) Imidacloprid/Permethrin/Pyriproxyfen: Acute Inhalation Toxicity Study in Rats-Limit Test	47014305	Bayer Healthcare LLC	PAY	
870.2400	Durando, J. (2006) Imidacloprid/Permethrin/Pyriproxyfen: Primary Eye Irritation Study in Rabbits	47014307	Bayer Healthcare LLC	PAY	
870.2500	Moore, G. (2006) Imidacloprid/Permethrin/Pyriproxyfen: Primary Skin Irritation Study in Rabbits	47014304	Bayer Healthcare LLC	PAY	
870.2600	Moore, G. (2006) Imidacloprid/Permethrin/Pyriproxyfen: Dermal Sensitization Study in Guinea Pigs (Buehler Method)	47014303	Bayer Healthcare LLC	PAY	

Signature:	Name and Title	Date
Kelly A. Hoskins	Kelly Hoskins, Manager of Regulatory Affairs	9/8/2016

Form Approved OMB No. 2070-0060

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401 M Street, S.W.
WASHINGTON, D.C. 20460

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DATA MATRIX

Date: September 8, 2016	EPA Reg No./File Symbol 2517-NEW	Page 2 of 4
Applicant's/Registrant's Name & Address Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	**Product**: Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs	

Ingredients: Imidacloprid, Permethrin, Pyriproxyfen

Guideline Reference No.	Guideline Study Name	MRID Number	Submitter	Status	Note
870.7200	**Companion Animal Safety**				
870.7200	Dandekar, D.; Schofield, J. (2006) Evaluation of the General Safety of Imidacloprid/Permethrin/Pyriproxyfen Spot-On Formulation in Adult Beagle Dogs (adult dogs)	47014309	Bayer Healthcare LLC	PAY	
870.7200	Dandkar, D.; Ciszewski, D. (2006) Evaluation of the General Safety of Imidacloprid/Permethrin/Pyriproxyfen Spot-On Formulation in 7 Week Old Puppies (puppies)	47014310	Bayer Healthcare LLC	PAY	
870.7200	Jones, R. (2001) Evaluation of the General Safety of 8.8% Imidacloprid with 44.0% Permethrin Formulation in the Target Species, 7-Week Old Puppies (puppies)	45563003	Bayer Healthcare LLC (K9 Advantix)	PAY	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Seven Week Old Puppies (puppies)	45097101	Bayer Healthcare LLC (Advantage PPF)	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Puppies: Lab Project Number: TR-96D-003: 74730: 10332. Unpublished study prepared by Bayer Corp. 47 p. (puppies)	44099801	Bayer Healthcare LLC (Advantage)	OLD	
870.7200	Acute Toxicity Evaluation for Dermal Treatment of Dogs with Imidacloprid (Bay t 7391) Spot-on: Lab Project Number: 74580: TR-94D-010. Unpublished study prepared by Miles Inc. 19 p. (adult dog)	43679607	Bayer Healthcare LLC (Advantage)	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Bay t 7391) Spot-On On Dogs: Lab Project Number: 74590: TR-95D-005. Unpublished study prepared by Bayer Corp. 40 p. (adult dog)	43679608	Bayer Healthcare LLC (Advantage)	OLD	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Adult Dogs (adult dog)	45097102	Bayer Healthcare LLC (Advantage PPF)	OLD	
870.7200	Mueller, R. (2001) General Safety of Imidacloprid with Permethrin Topical Solution in the Dog (adult dog)	45563002	Bayer Healthcare LLC	PAY	
Pyriproxyfen Generic Data for Companion Animal Use					
	Evaluation of the Toxicology and Potential Health Risks Associated with Indoor, Nonfood Uses of Sumilarv; J. Driver, S. Oonnithan, O. Paynter, et al. (1991) Unpublished study prepared by Technology Services Group. Inc. 71 p.	42182701	McLaughlin Gormley King Company	OLD	PPF

Signature:	Name and Title	Date
Kelly A Hoskins	Kelly Hoskins, Manager of Regulatory Affairs	9/8/2016

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WASHINGTON, D.C. 20460

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DATA MATRIX

Date: September 8, 2016	EPA Reg No./File Symbol 2517-NEW	Page 3 of 4
Applicant's/Registrant's Name & Address Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	**Product:** Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs	

Ingredients: Imidacloprid, Permethrin, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	S31183: Toxicity Study by Oral (Capsule) Administration to Beagle Dogs for 52 Weeks (Sumilarv Technical Grade): Lab Project Number: 91/0776. Unpublished study prepared by Life Science Research Ltd. 320 p.	42178309	McLaughlin Gormley King Company	OLD	PPF
810.3300	**Efficacy**				
810.3300	Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs: (Final Report) (speed of kill)	44256901	Bayer Healthcare LLC (Advantage)	OLD	
810.3300	Imidacloprid Topical Formulation: Larvicidal Effect Against Ctenocephalides felis in the Surroundings of Treated Dogs (flea larvae)	44256902	Bayer Healthcare LLC (Advantage)	OLD	
810.3300	Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs (shampoo)	44256903	Bayer Healthcare LLC (Advantage)	OLD	
810.3300	Cunningham, J. (2001) Efficacy of Topically Applied Imidacloprid and Permethrin Against Flea (Ctenocephalides felis) and Tick (Rhipicphalus sanguineus) Infestations on Dogs (brown dog tick)	45563011	Bayer Healthcare LLC (Advantix)	PAY	
810.3300	Young, D. (2001) Final Report: Efficacy of Topically Applied Imidacloprid + Permethrin Against Flea (Ctenocephalides felis) and Tick (Amblyomma americanum) Infestations on Dogs (lone star tick)	45573501	Bayer Healthcare LLC (Advantix)	PAY	
810.3300	Fourie, L. (2004) Assessment of the Efficacy of an Imidacloprid (10%) / Permethrin (50%) Spot-On against Stomoxys calcitrans on Dogs (biting flies)	46978901	Bayer Healthcare LLC	PAY	
810.3300	Fourie, L.; Stanneck, D. (2005) Assessment of the Efficacy of an Imidacloprid 10% / Permethrin 50% Spot-On against Stomoxys calcitrans on Dogs (biting flies)	46978902	Bayer Healthcare LLC	PAY	
810.3300	Cunningham, J.; Everett, R. (2002) Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of K9 Advantix for Flea and Tick Control on Dogs (waterproof)	47109101	Bayer HealthCare LLC	PAY	

Signature:	Name and Title	Date
Kelly R. Hoskins	Kelly Hoskins, Manager of Regulatory Affairs	9/8/2016

Form Approved OMB No. 2070-0060

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DATA MATRIX

Date: September 8, 2016	EPA Reg No./File Symbol 2517-NEW	Page 4 of 4
Applicant's/Registrant's Name & Address Sergeant's Pet Care Products, Inc. 10077 South 134th Street Omaha, NE 68138	**Product:** Sergeant's Imidacloprid + Permethrin + Pyriproxyfen Squeeze On for Dogs	

Ingredients: Imidacloprid, Permethrin, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Cunningham, J.; Everett, R.; Arther, R.; et al. (2002) Addendum 1 to: Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of K9 Advantix for Flea and Tick Control on Dogs (Protocol and Raw Data) (waterproof)	47298201	Bayer HealthCare LLC	PAY	
810.3300	Pennington, R.; Cruthers, L. (1994) Study Report for the Efficacy Evaluation of ECTO Flea and Tick Insecticide with IGR for Fleas, Ticks, and Mosquitoes (permethrin)	43396409	Ecto Development Corporation	OLD	
810.3300	Pennington, R.; Cunningham, J. (1994) Study Report for the Efficacy Evaluation of ECTO Flea and Tick Insecticide with IGR for Fleas and Ticks (permethrin)	43396410	Ecto Development Corporation	OLD	
810.3300	Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p. (PPF)	45086801	McLaughlin Gormley King Company	OLD	
810.3300	Cunningham, J. (1995) Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Dogs (fleas)	43679609	Bayer Healthcare LLC (Advantage)	OLD	
810.3300	Cunningham, J.; Everett, R. (1994) Efficacy Confirmation of NTN 33893 (Imidacloprid) Solution Applied Dermally for Control of Fleas on Dogs (fleas)	43679610	Bayer Healthcare LLC (Advantage)	OLD	
810.3300	Doyle, J.; Egan, T. (2006) A Controlled Randomised Study to Evaluate the Efficacy of Advantage Against a Natural Infestation of Dog Lice (Trichodectes canis) Following a Single Topical Administration to Adult Mixed Breed Dogs (lice)	47190401	Bayer Healthcare LLC (Advantage)	PAY	

Signature:	Name and Title	Date
Kelly R Hoskins	Kelly Hoskins, Manager of Regulatory Affairs	9/8/2016

Pages 111-112 *CSF may be entitled to confidential treatment*